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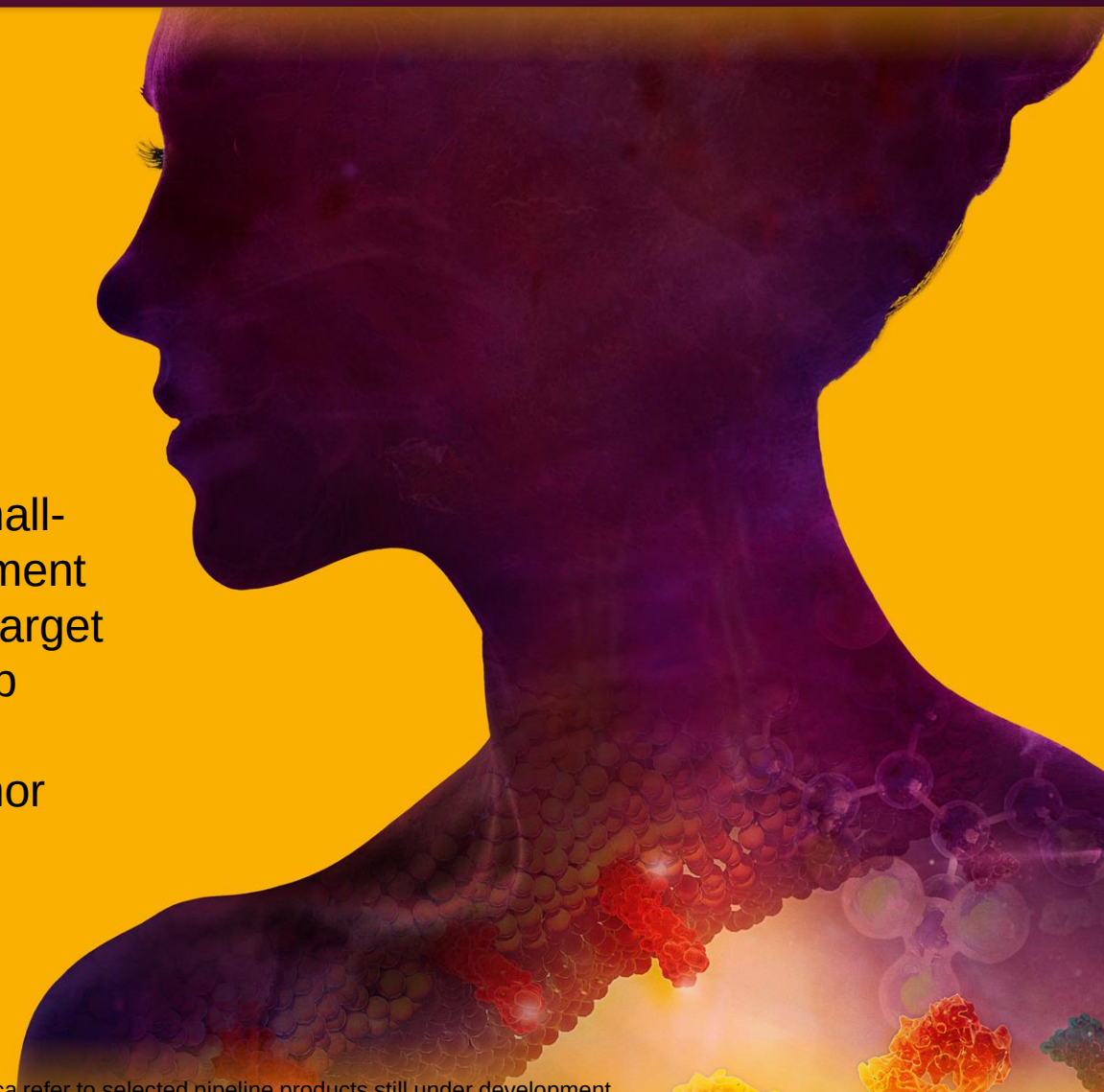
Oncology Portfolio

What science can do

AstraZeneca is investigating combinations of biologic and small-molecule therapies for the treatment of cancer. These combinations target the tumor directly and some help boost the body's own immune system to potentially induce tumor cell death.



Any compounds illustrated from AstraZeneca refer to selected pipeline products still under development.
AstraZeneca pipeline products are investigational products and, as such, are not approved by the US Food and Drug Administration, European Medicines Agency, or any other regulatory agency for the uses under investigation. Information regarding these investigational products should under no circumstances be regarded as a recommendation for their use or of their safety or efficacy.

The Future of Oncology

Putting the patient first
Explore our portfolio by **tumor type**

What science can do
Explore our portfolio by **cell pathway**

Research & development
Explore our portfolio by **clinical phase**

Immuno-Oncology

Activating and directing the immune system to fight cancer

View all abbreviations & acronyms

Target	Compound	Area Under Investigation	Phase
PD-L1 inhibition	Durvalumab	NSCLC SCLC HNSCC Advanced solid tumors Bladder cancer Hepatocellular carcinoma Pancreatic ductal carcinoma Hematologic malignancies TNBC Cervical cancer Prostate cancer Colorectal cancer Ovarian cancer BTK Endometrial cancer	III III III III III III II I II III II II III III III
CTLA-4 inhibition	Tremelimumab	Advanced solid tumors	III
PD-1/CTLA-4 bispecific mAb	MEDI5752	Advanced solid tumors	I
A2AR antagonism	AZD4635	Advanced solid tumors Prostate cancer	I II
CD73 inhibition	Oleclumab (MEDI9447)	Solid tumors NSCLC Advanced pancreatic cancer Metastatic TNBC Prostate Colorectal	I II II II I II
NKG2A inhibition	Monalizumab[a]	Advanced solid tumors NSCLC HNSCC Colorectal	II II II II
CD39 inhibition	IPH5201[b]	Advanced solid tumors	I
NDV GM-CSF	MEDI5395	Advanced solid tumors	I
IL12 mRNA	MEDI1191	Advanced solid tumors	I
Plasmid DNA Vaccine	MEDI0457[c]	HPV-16/18+ HNSCC	II

[a]Monalizumab is partnered with Innate Pharma; [b]Partnered asset; [c]Therapeutic vaccine for HPV-16/18+ cancers is developed in partnership with Inovio Pharmaceuticals, Inc.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

View all abbreviations & acronyms

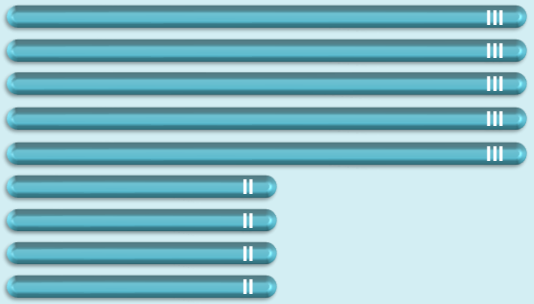
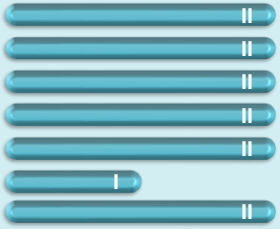
Target	Compound	Area Under Investigation	Phase
EGFR-TKI inhibition	Osimertinib	Advanced metastatic EGFRm NSCLC	III
VEGFR tyrosine kinase inhibition	Cediranib	Platinum-resistant ovarian cancer Platinum-sensitive ovarian cancer Advanced solid tumors	III III II
MEK inhibition	Selumetinib[a]	Neurofibromatosis type 1 (NF1)	II
AKT inhibition	Capivasertib[b]	Breast cancer Prostate cancer	III II
MET inhibition	Savolitinib/volitinib[c]	EGFRm NSCLC MET-driven NSCLC	I II
PI3K β/δ inhibition	AZD8186	Advanced solid tumors	I
ERα degradation and antagonism	AZD9833	ER+, HER2- breast cancer	II
BTK inhibition	Acalabrutinib[d]	Hematologic malignancies	III
MCL1 inhibition	AZD5991	R/R hematologic malignancies	I
CDK9 inhibition	AZD4573	R/R hematologic malignancies	I
BRD4 inhibition	AZD5153	Advanced solid tumors Hematologic malignancies	I I
BCL2/BCL-XL inhibition	AZD0466	Advanced solid tumors Hematologic malignancies	I I

[a]Selumetinib is licensed from Array BioPharma Inc; [b]Formerly known as AZD5363: discovered by AstraZeneca subsequent to a collaboration with Astex Therapeutics (and its collaboration with the Institute of Cancer Research and Cancer Research Technology Limited); [c]Partnered with Hutchison MediPharma Limited; [d]Developed in collaboration with Acerta Pharmaceuticals.

DNA Damage Response

Exploiting pathway dependencies to potentially induce cancer death

View all abbreviations & acronyms

Target	Compound	Area Under Investigation	Phase
PARP inhibition	Olaparib[a]	Ovarian cancer Breast cancer Pancreatic cancer Colorectal cancer Prostate cancer Advanced solid tumors Gastric cancer NSCLC Bladder cancer	
WEE1 kinase inhibition	Adavosertib (AZD1775)[b]	SCLC Solid tumors Bladder cancer	
ATR kinase inhibition	Ceralasertib (AZD6738)	Solid tumors Ovarian Breast cancer HNSCC NSCLC Hematologic malignancies SCLC	
AURKB inhibition	AZD2811 nanoparticle	Advanced solid tumors Hematologic malignancies	
ATM inhibition	AZD1390	CNS malignancies	
DNA-PK inhibition	AZD7648	Advanced solid tumors	

[a]In collaboration with Merck & Co., Inc., Kenilworth, NJ, US (Merck: known as MSD outside the US and Canada); [b]In-licensed from Merck & Co., Inc. (MSD).

Antibody Drug Conjugates

Innovative approaches to selectively deliver cytotoxic payloads to tumors

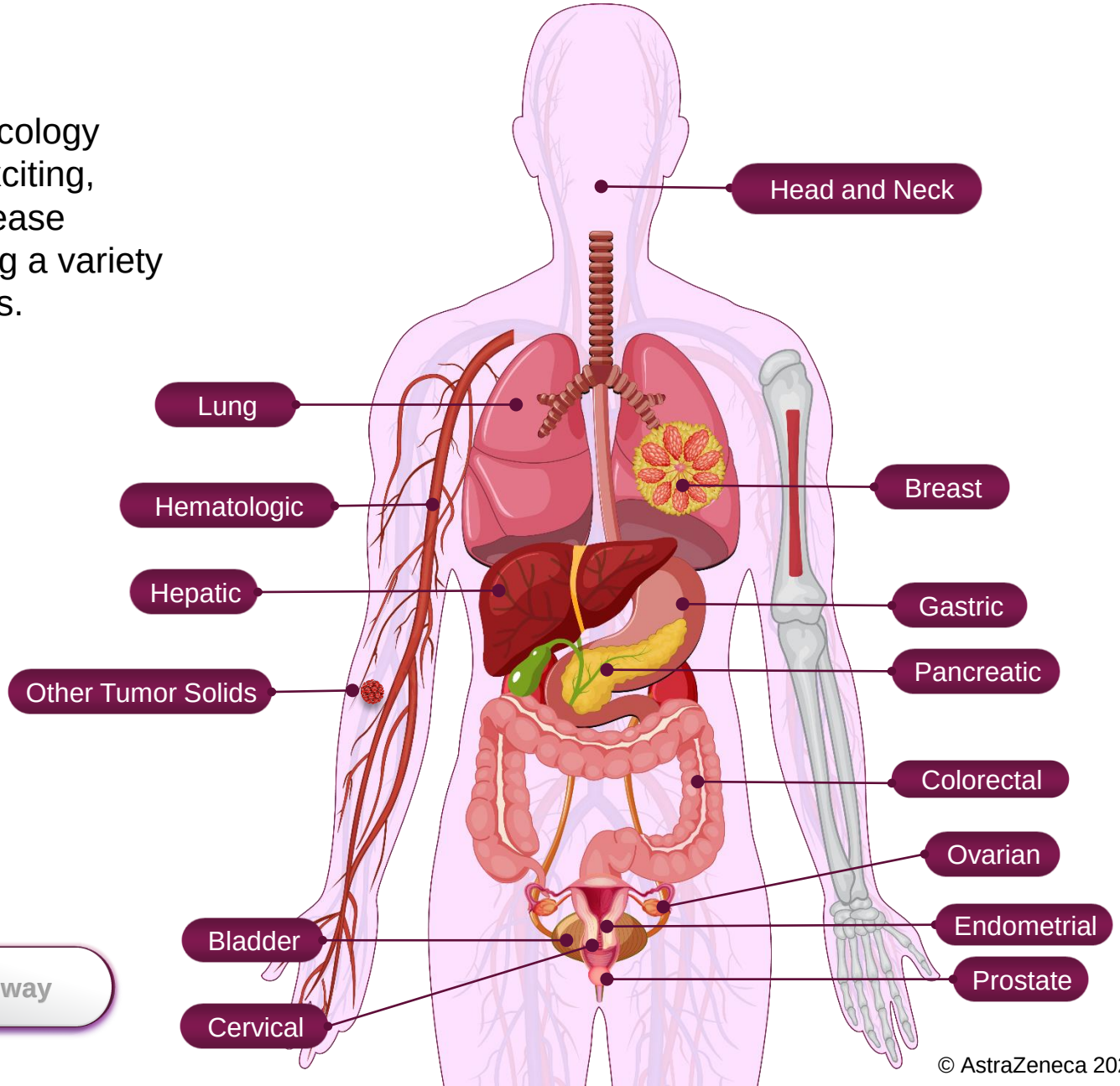
View all abbreviations & acronyms

Target	Compound	Area Under Investigation	Phase
Anti-BCMA ADC	MEDI2228	Relapsed/refractory multiple myeloma	I
Anti-HER2 ADC	Trastuzumab deruxtecan[a,b] (formerly DS-8201)	Breast cancer	III
		Colorectal cancer	II
		Gastric/GEJ cancer	II
		NSCLC	II
		Bladder cancer	II
		Advanced solid tumors	I

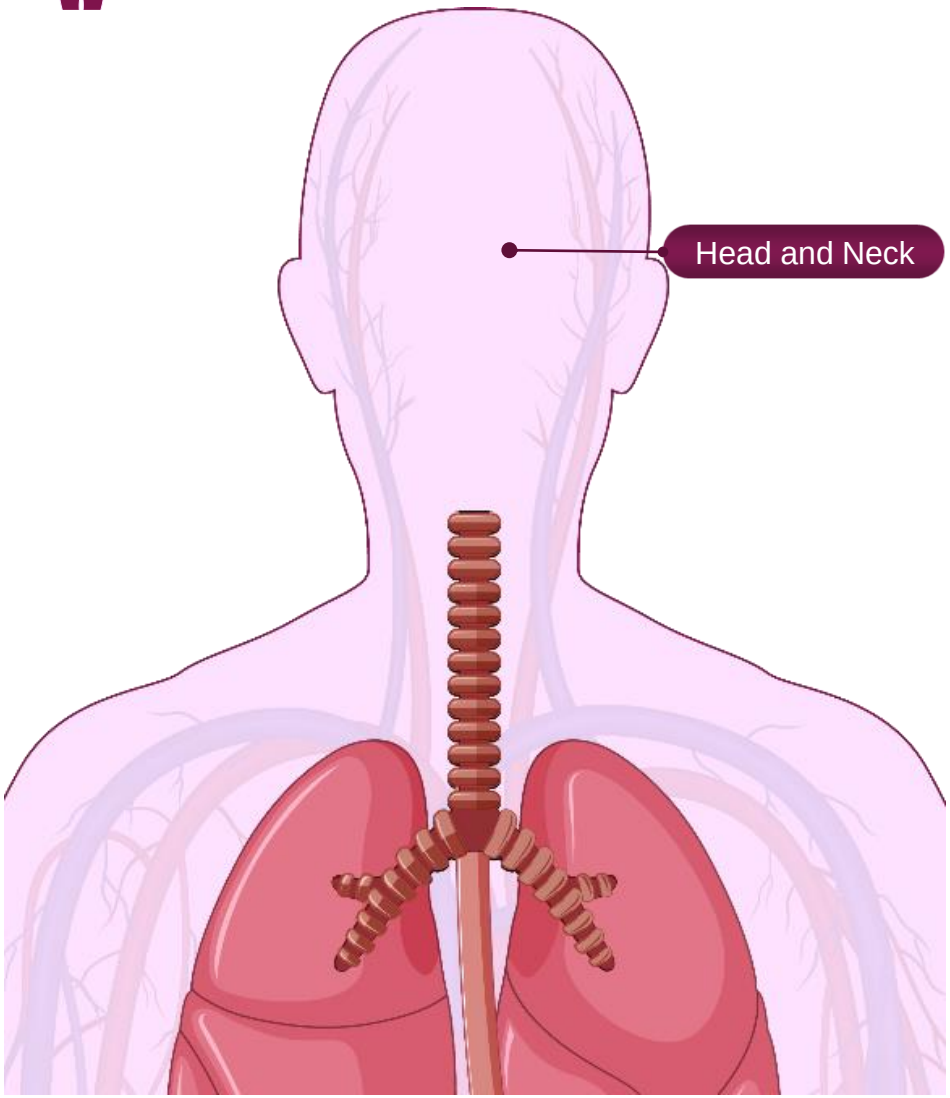
[a]In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US
[b]fam-trastuzumab deruxtecan-nxki in US only; trastuzumab deruxtecan in other regions of world. Trademark belongs to Daiichi Sankyo.

Tumor Type

Our industry-leading oncology pipeline is broad and exciting, addressing multiple disease pathways and evaluating a variety of combination therapies.



Tumor Type | Cell Pathway

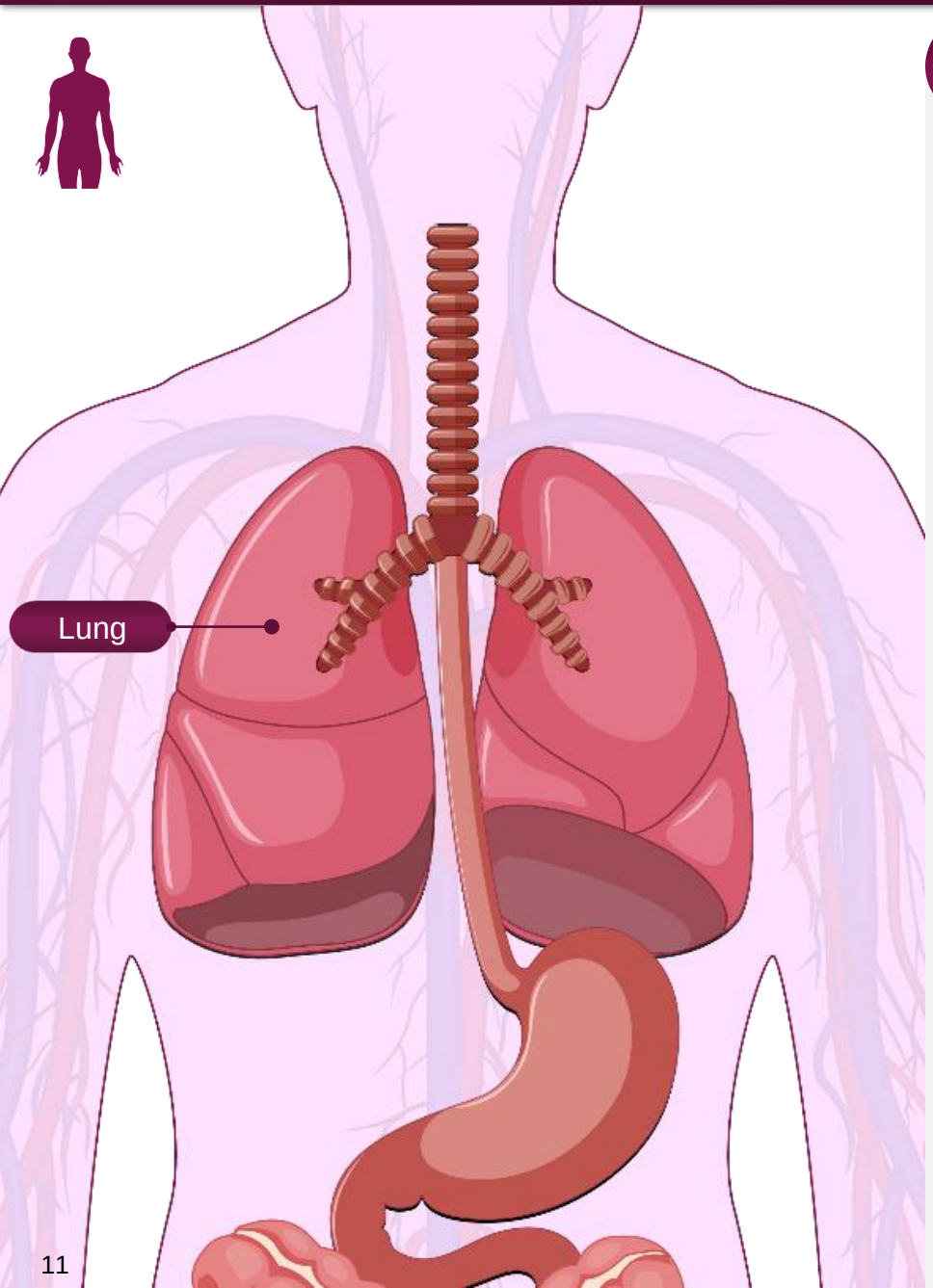


Head and Neck

Investigational Molecules

Mechanism	Compound	Phase
PD-L1 inhibition	Durvalumab	I-III
CTLA-4 inhibition	Tremelimumab	I-III
NKG2A inhibition	Monalizumab	I-II
ATR kinase inhibition	Ceralasertib[a]	I-II
Plasmid DNA vaccine	MEDI0457	I-II

[a]Previously known as AZD6738.

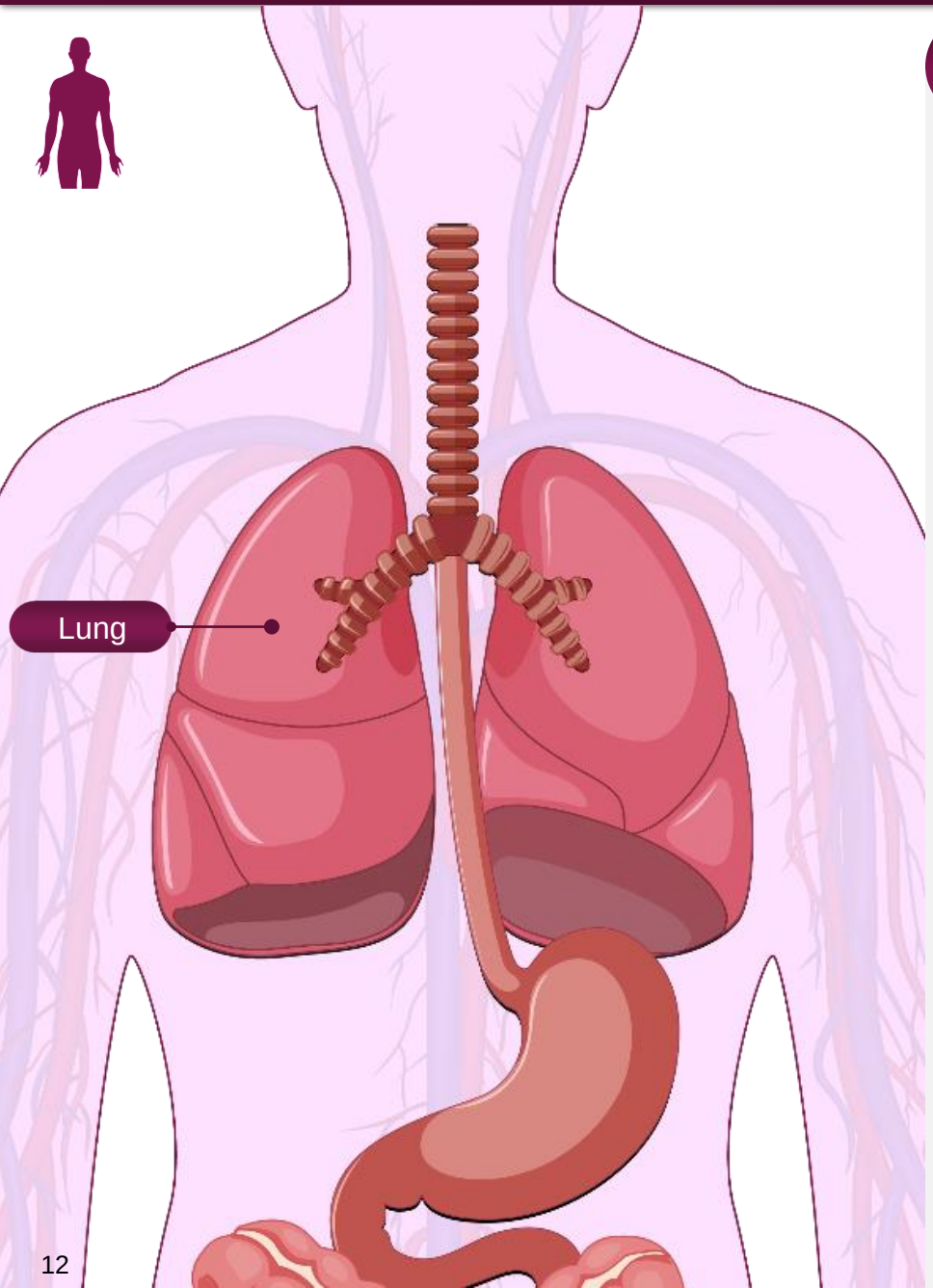


Lung

Investigational Molecules

Mechanism	Compound	Phase
PD-L1 inhibition	Durvalumab	I-III
CTLA-4 inhibition	Tremelimumab	I-III
EGFR-TKI inhibition: Activating and T790M mutations	Osimertinib	I-III
MET inhibition	Savolitinib	I-II
AURKB inhibition	AZD2811 nanoparticle	I
ATR kinase inhibition	Ceralasertib[a]	I-II
WEE1 kinase inhibition	Adavosertib[b]	II

[a]Previously known as AZD6738; [b]Previously known as AZD1775, in-licensed from Merck & Co., Inc. (MSD).

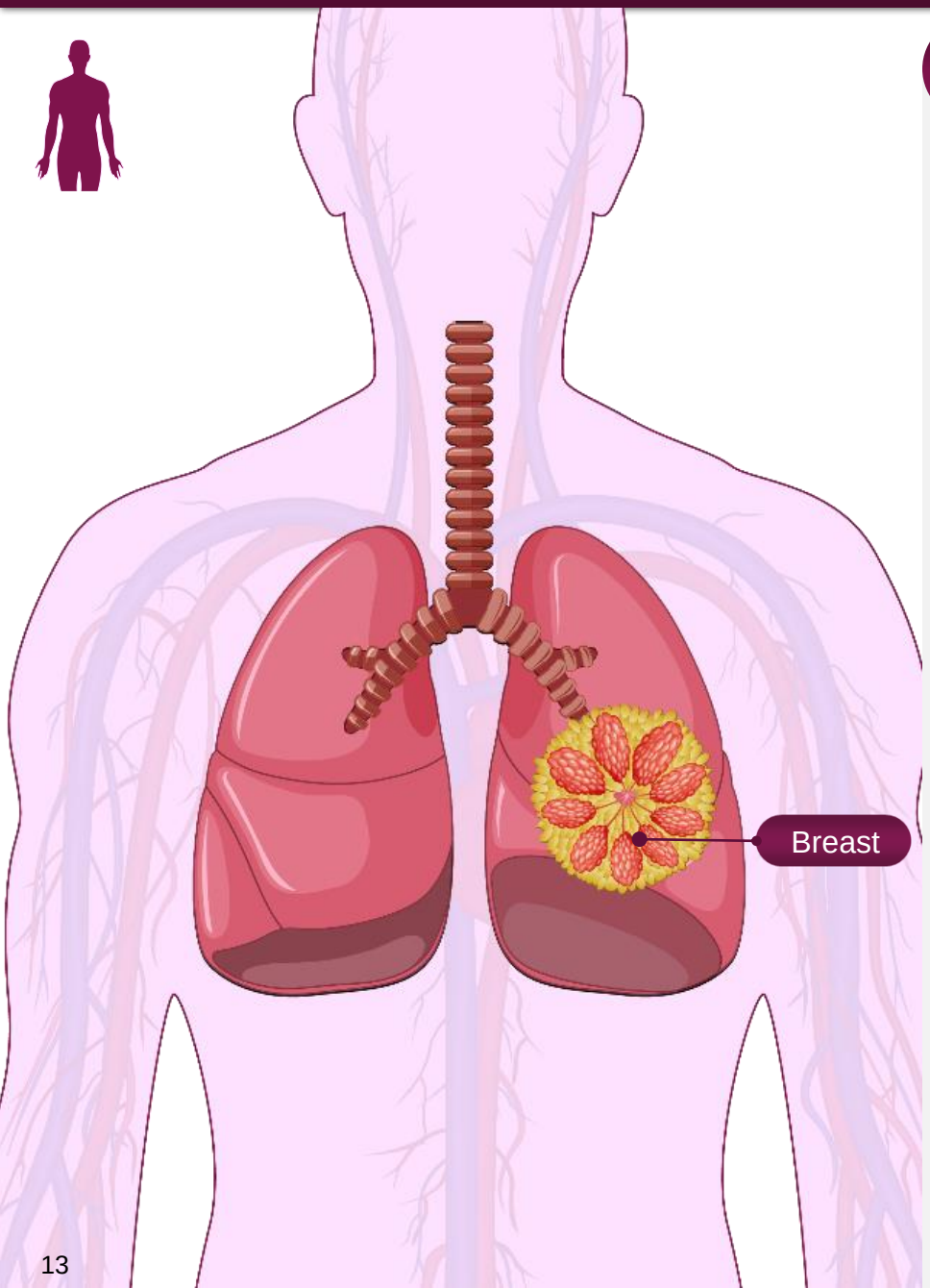


Lung (cont'd.)

Investigational Molecules

Mechanism	Compound	Phase
PARP inhibition	Olaparib	I-II
CD73 inhibition	Oleclumab[a]	I-II
Anti-HER2 ADC	Trastuzumab deruxtecan[b] (DS-8201)	II
NKG2A inhibition	Monalizumab	II

[a]Previously known as MEDI9447; [b]In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US.

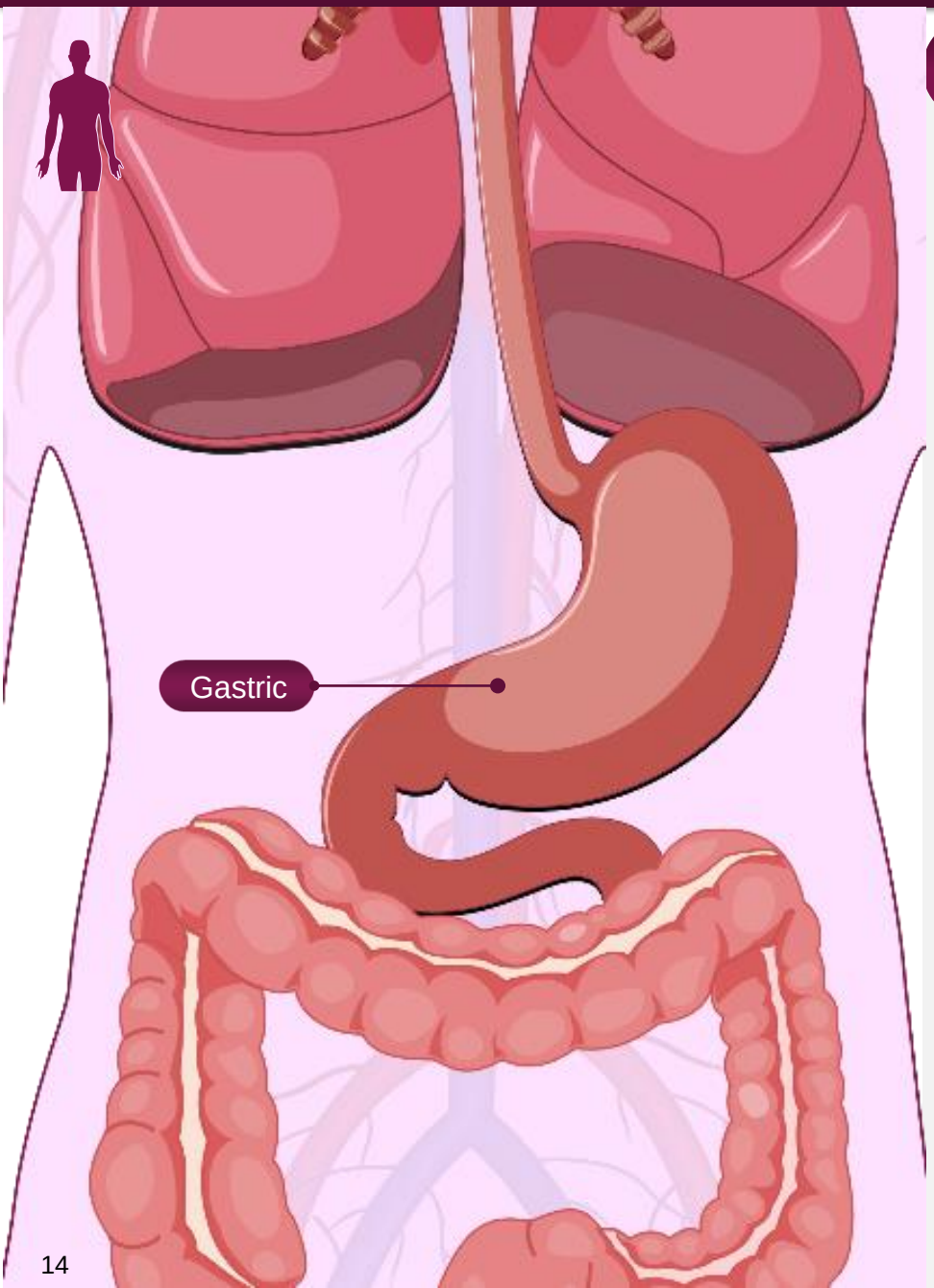


Breast

Investigational Molecules

Mechanism	Compound	Phase
AKT inhibition	Capivasertib[a]	I-II
ERα degradation and antagonism	AZD9833	II
PARP inhibition	Olaparib[b]	I-III
ATR kinase inhibition	Ceralasertib[c]	II
WEE1 Kinase inhibition	Adavosertib[d]	II
CD73 inhibition	Oleclumab	II
PD-L1 Inhibition	Durvalumab	I-II
Anti-HER2 ADC	Trastuzumab deruxtecan[e] (DS 8201)	I-III

[a]Formerly known as AZD5363, discovered by AstraZeneca subsequent to a collaboration with Astex Therapeutics and its collaboration with the Institute of Cancer Research and Cancer Research Technology Limited); [b]In collaboration with Merck & Co., Inc. (MSD); [c]Previously known as AZD6738; [d]Formerly known as AZD1775, in-licensed from Merck and Co. Inc. (MSD); [e]In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US.

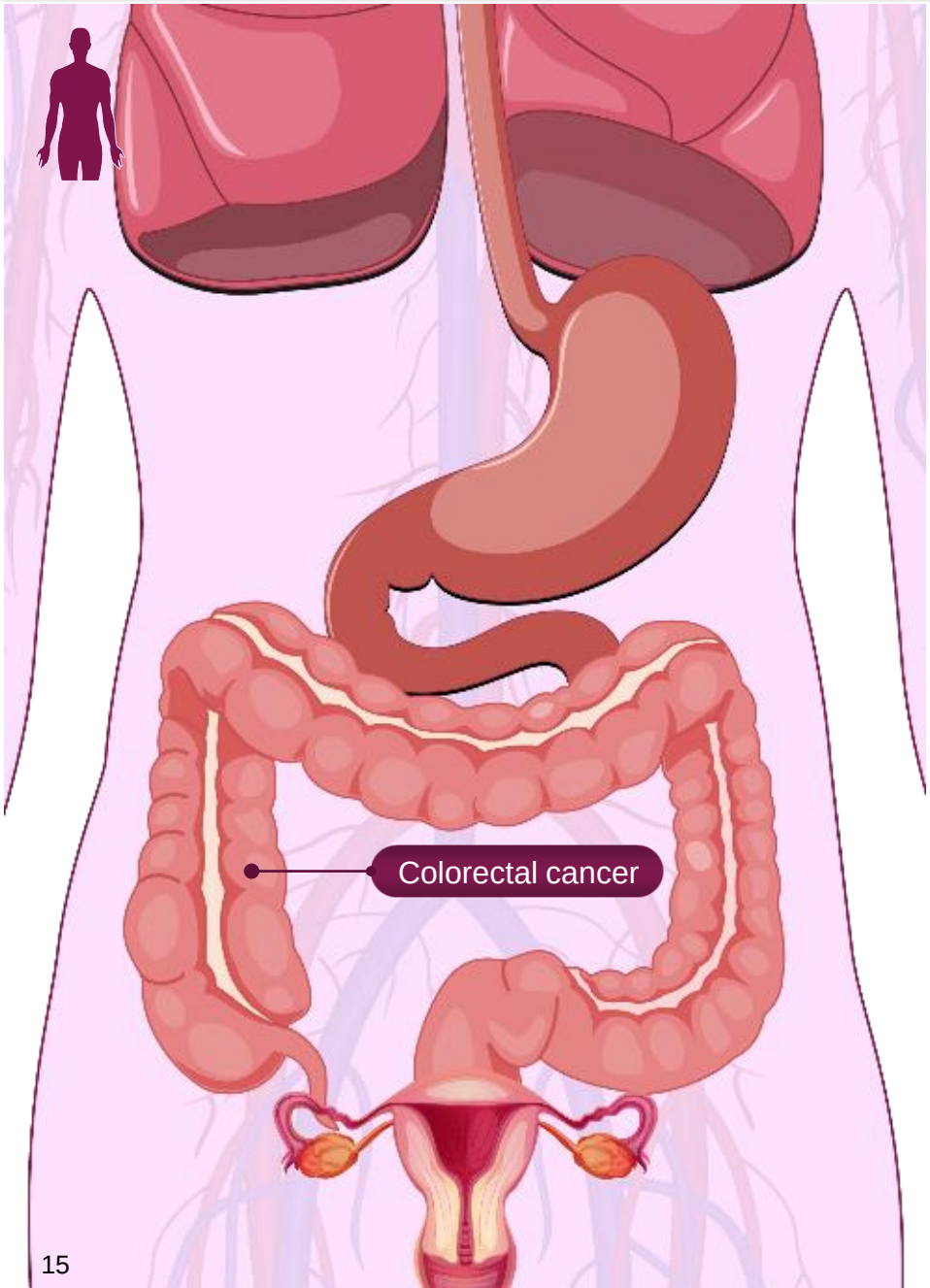


Gastric

Investigational Molecules

Mechanism	Compound	Phase
PARP inhibition	Olaparib[a]	I-II
Anti-HER2 ADC	Trastuzumab deruxtecan[b] (DS-8201)	I-III

[a]In collaboration with Merck & Co., Inc. (MSD); [b]In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US.

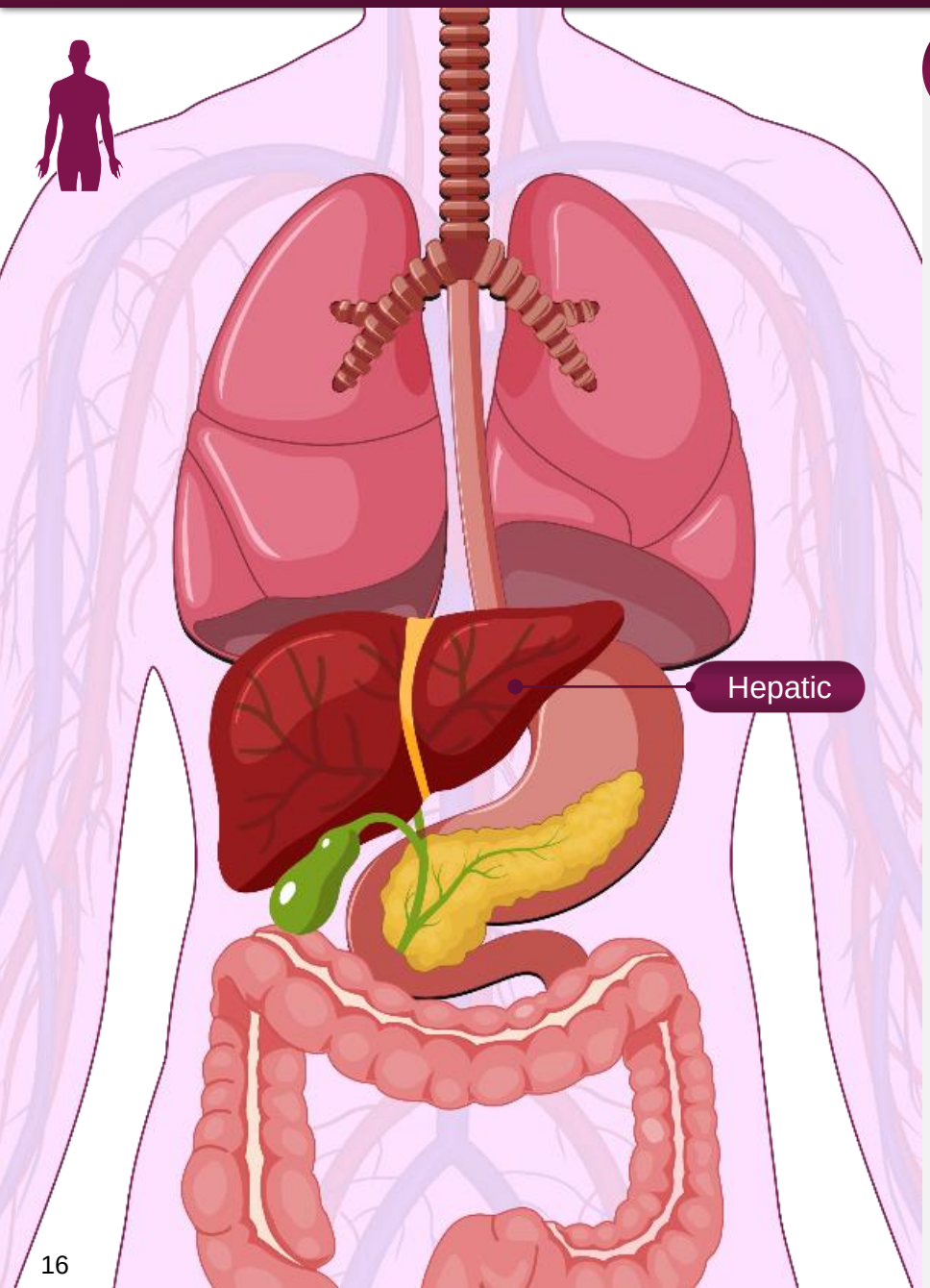


Colorectal

Investigational Molecules

Mechanism	Compound	Phase
Anti-HER2 ADC	Trastuzumab deruxtecan[a] (DS-8201a)	II
NKG2A inhibition	Monalizumab[b]	I-II
CD73 inhibition	Oleclumab	II
PD-L1 inhibition	Durvalumab	I-II
PARP inhibition	Olaparib	III

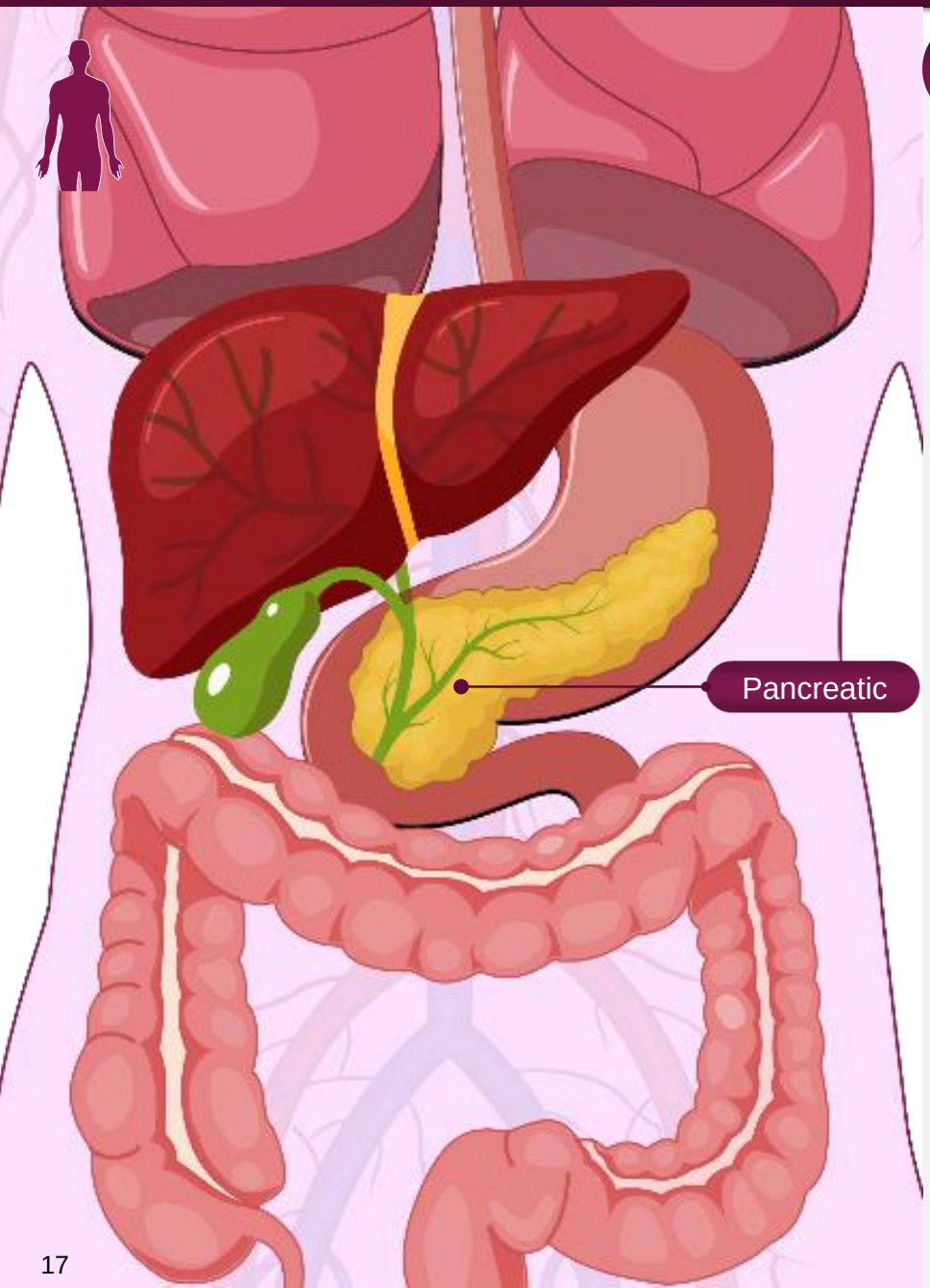
[a]In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US; [b]Partnered with Innate Pharma.



Hepatic

Investigational Molecules

Mechanism	Compound	Phase
PD-L1 inhibition	Durvalumab	III
CTLA-4 inhibition	Tremelimumab	III

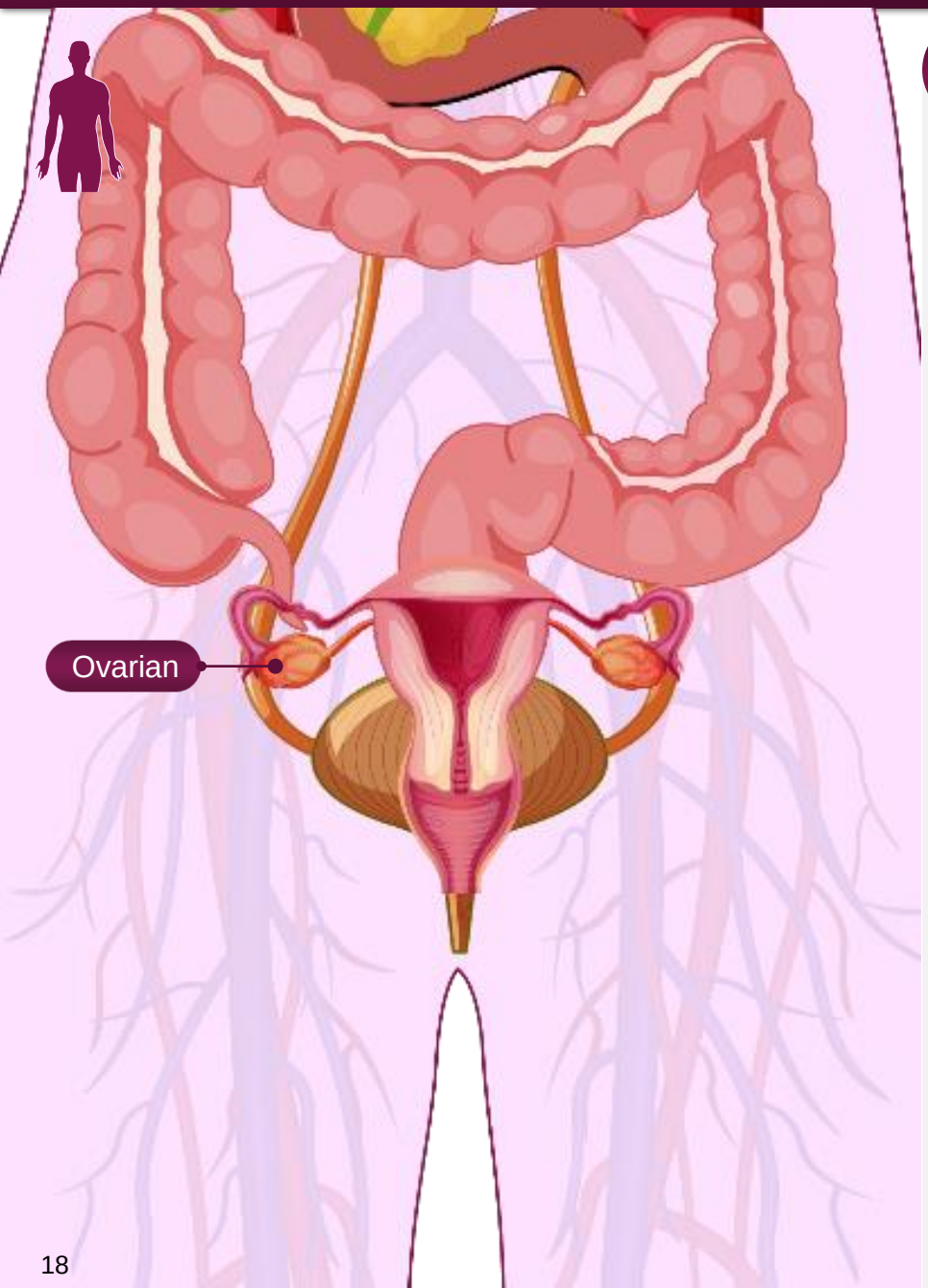


Pancreatic

Investigational Molecules

Mechanism	Compound	Phase
PARP inhibition	Olaparib[a]	II-III
PD-L1 inhibition	Durvalumab	I-II
CTLA-4 inhibition	Tremelimumab	II
CD73 inhibition	Oleclumab	II

[a]In collaboration with Merck & Co., Inc. (MSD).

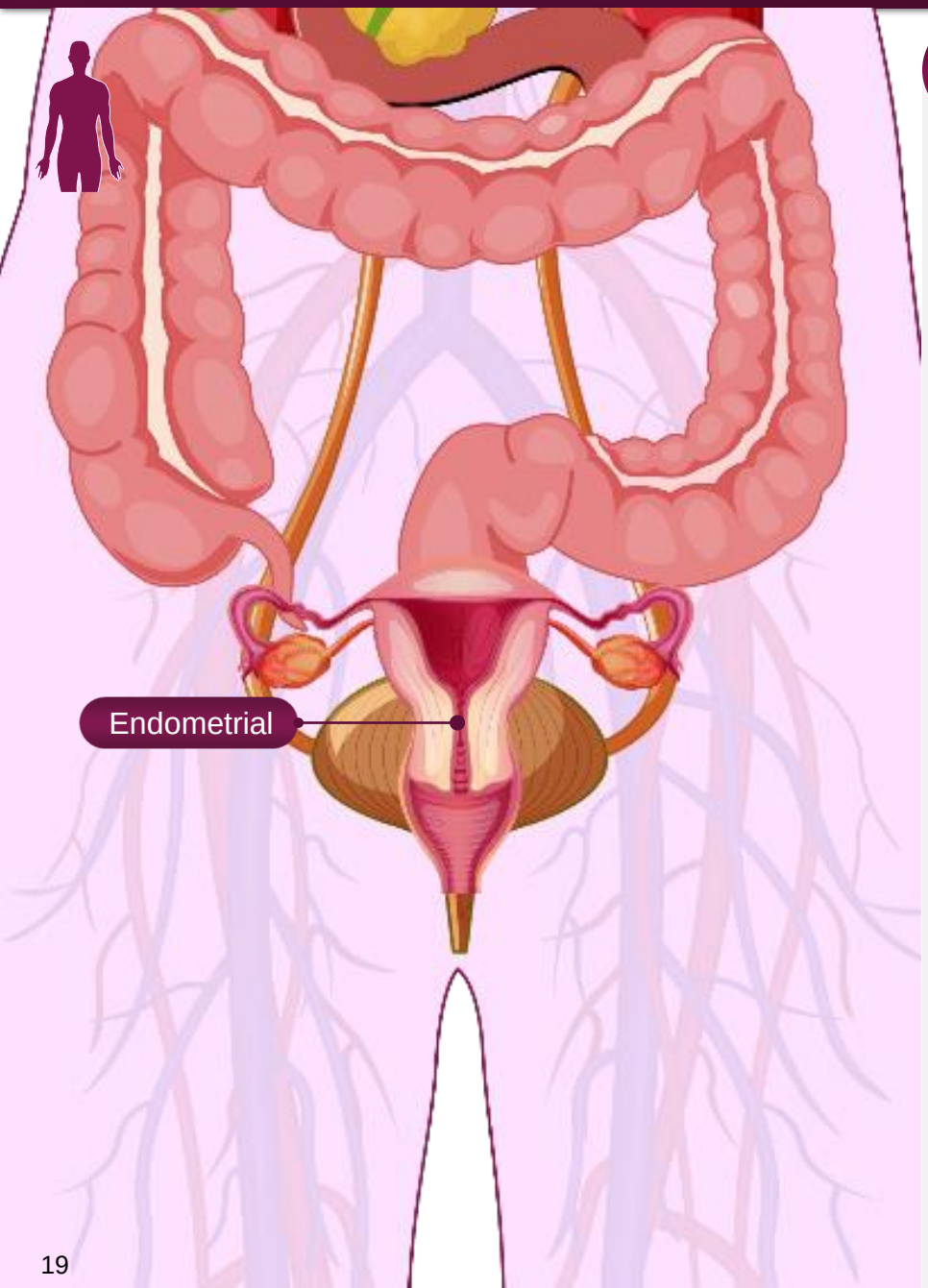


Ovarian

Investigational Molecules

Mechanism	Compound	Phase
PARP inhibition	Olaparib[a]	II-III
ATR kinase inhibition	Ceralasertib	II
VEGFR tyrosine kinase inhibition	Cediranib	I-III
PD-L1 inhibition	Durvalumab	III

[a]In collaboration with Merck & Co., Inc. (MSD)

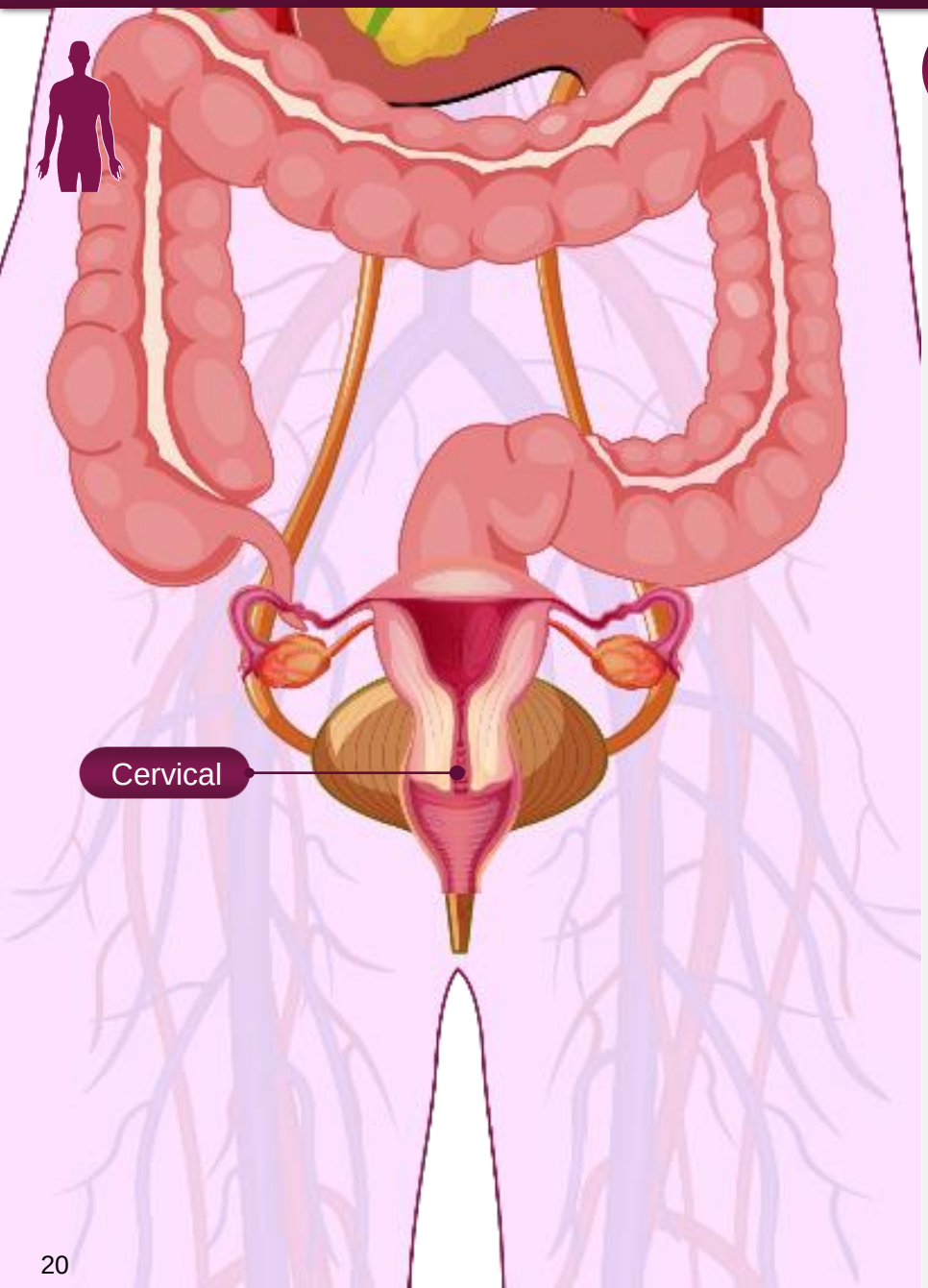


Endometrial

Investigational Molecules

Mechanism	Compound	Phase
PARP inhibition	Olaparib[a]	III
PD-L1 inhibition	Durvalumab	III

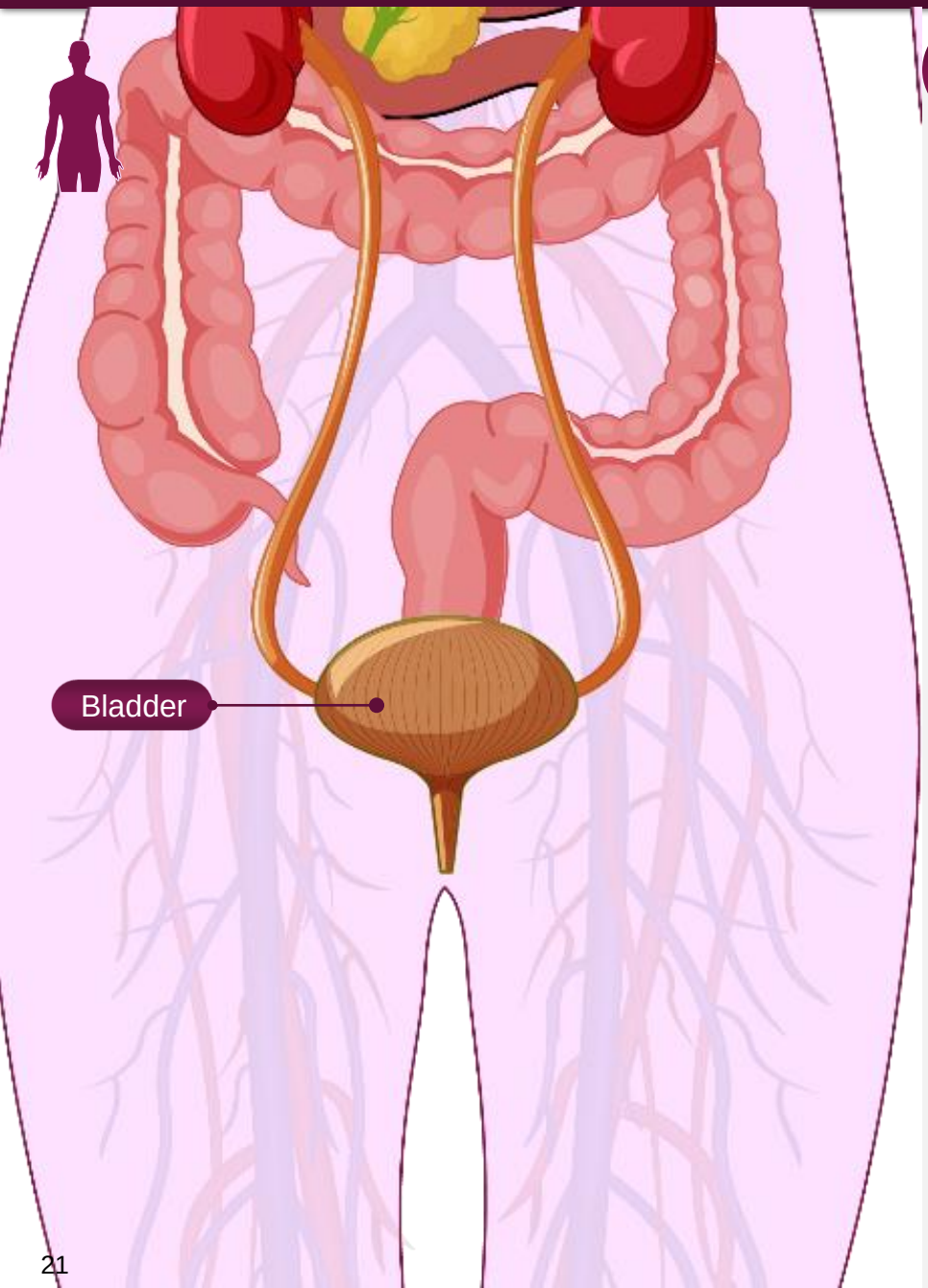
[a]In collaboration with Merck & Co., Inc. (MSD).



Cervical

Investigational Molecules

Mechanism	Compound	Phase
PD-L1 inhibition	Durvalumab	III

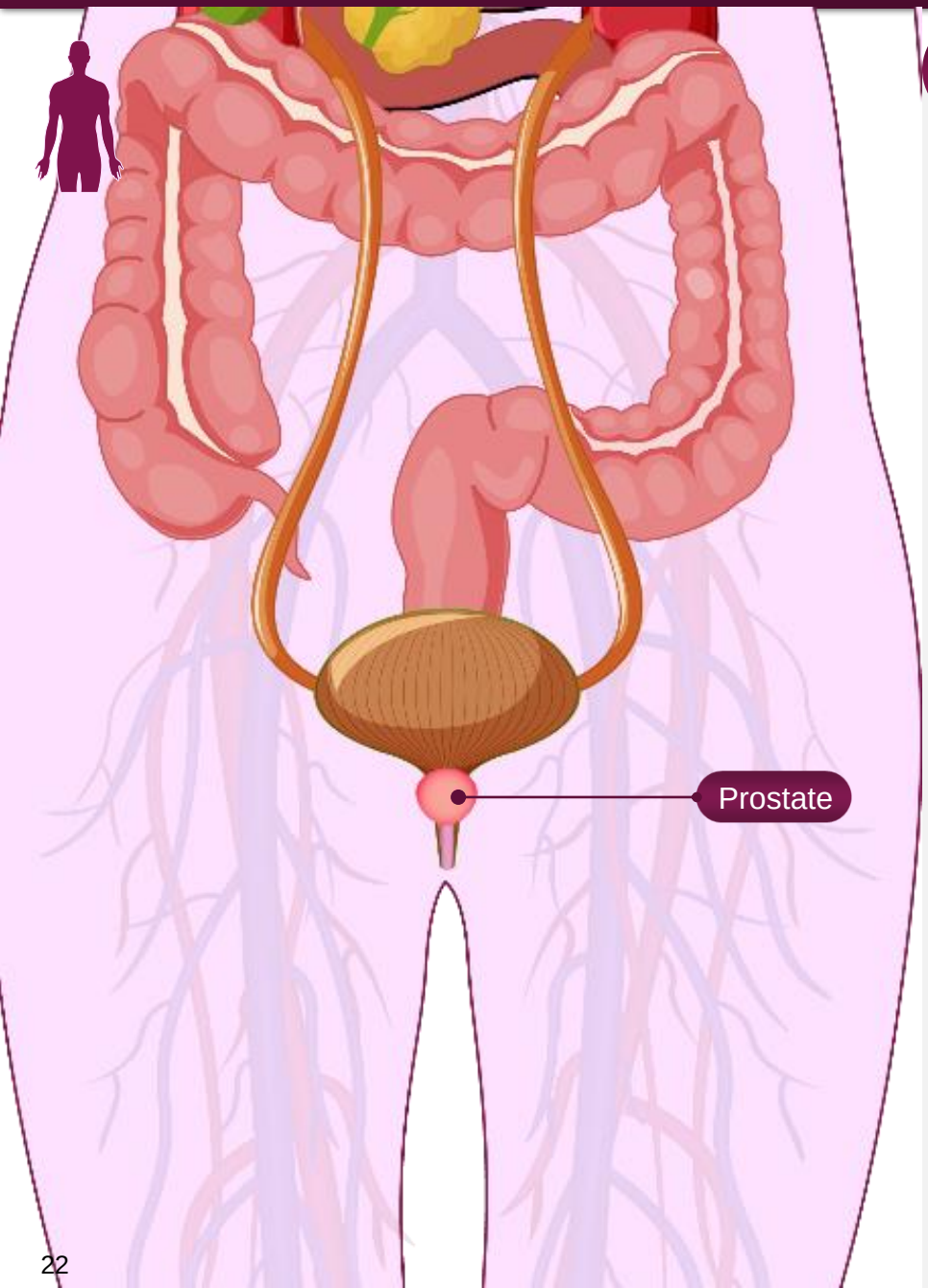


Bladder

Investigational Molecules

Mechanism	Compound	Phase
PD-L1 inhibition	Durvalumab	I-III
CTLA-4 inhibition	Tremelimumab	I-III
WEE1 kinase inhibition	Adavosertib[a]	I
PARP inhibition	Olaparib[b]	II
Anti-HER2	Trastuzumab deruxtecan[c] (DS-8201)	I-II

[a]Previously known as AZD1775, in-licensed from Merck & Co., Inc; [b]In collaboration with Merck & Co., Inc. (MSD); [c]In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US.

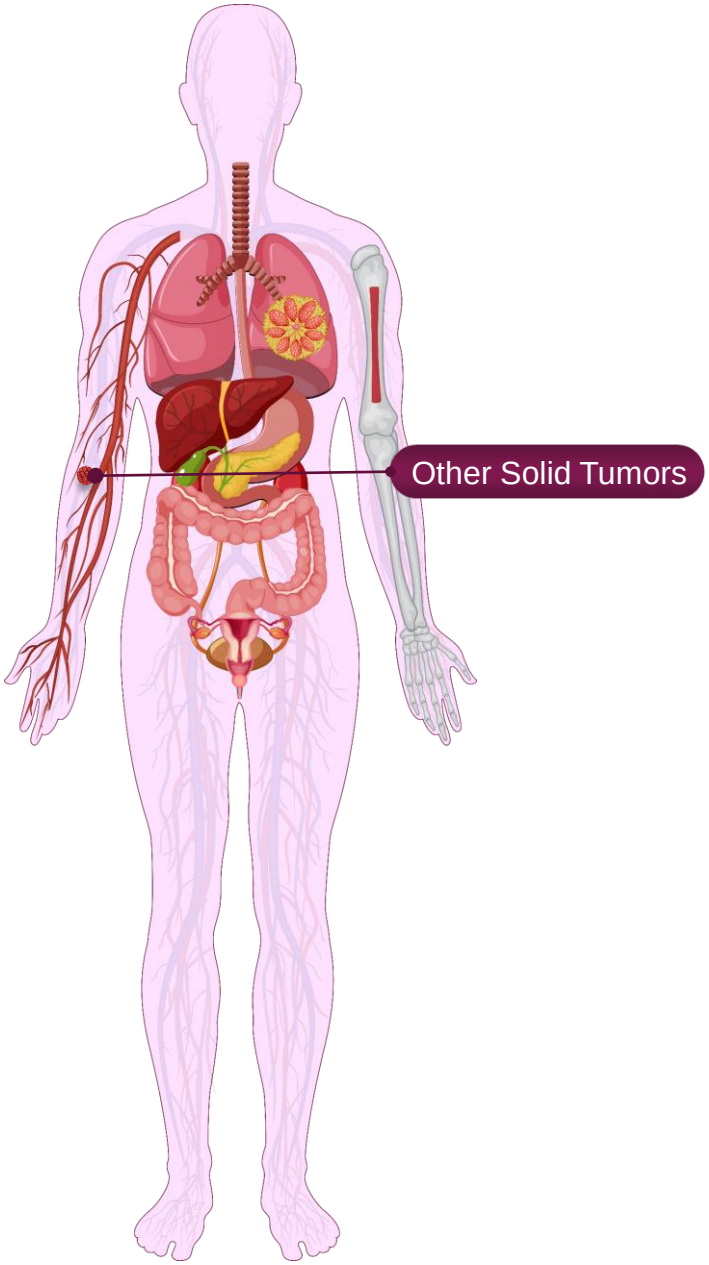


Prostate

Investigational Molecules

Mechanism	Compound	Phase
AKT inhibition	Capivasertib[a]	I-II
A2AR inhibition	AZD4635	II
PARP inhibition	Olaparib[b]	II-III
PD-L1 inhibition	Durvalumab	II
CD73 inhibition	Oleclumab	II

[a]Previously known as AZD5363, discovered by AstraZeneca subsequent to a collaboration with Astex Therapeutics (and its collaboration with the Institute of Cancer Research and Cancer Research Technology Limited); [b]In collaboration with Merck & Co., Inc. (MSD).

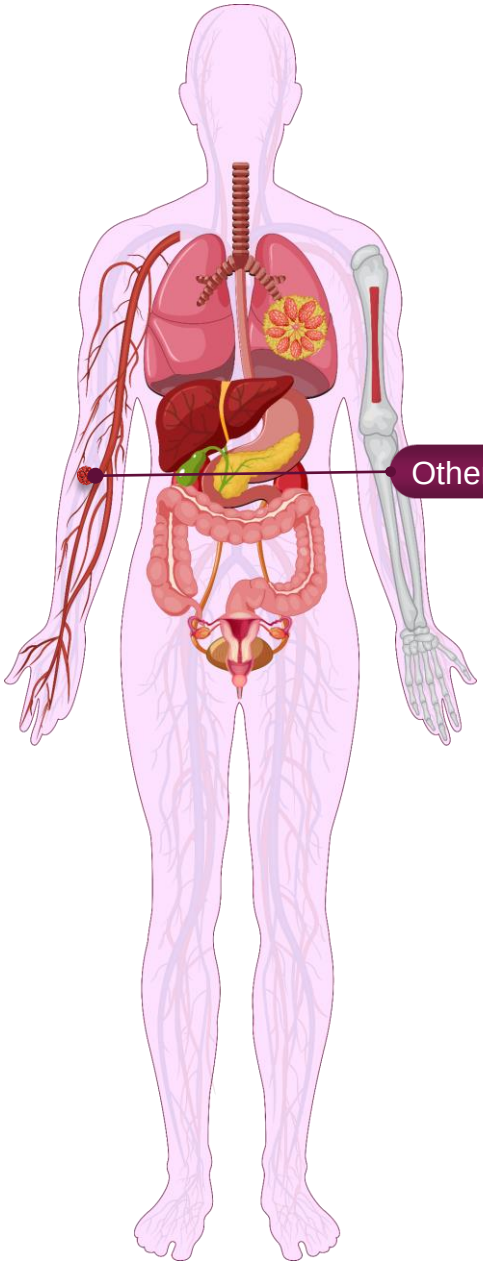


Other Solid Tumors

Investigational Molecules

Mechanism	Compound	Phase
PD-L1 inhibition	Durvalumab	I-III
CTLA-4 inhibition	Tremelimumab	II
A2AR antagonism	AZD4635	I
CD73 inhibition	Oleclumab	I
NKG2A inhibition	Monalizumab[a]	I
CD39 inhibition	IPH5201	I
PI3K β/δ inhibition	AZD8186	I
DNA-PK inhibition	AZD7648	I-II
AKT inhibition	Capivasertib	I

[a]Partnered with Innate Pharma

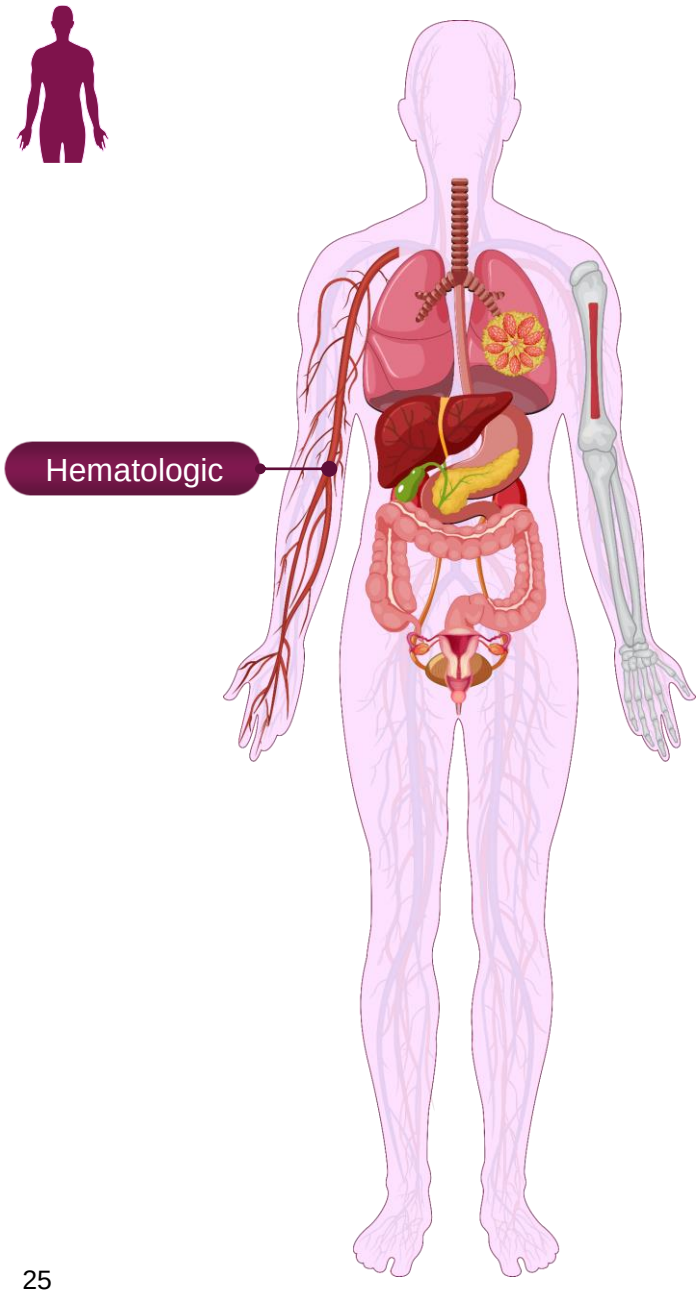


Other Solid Tumors (cont'd.)

Investigational Molecules

Mechanism	Compound	Phase
WEE1 kinase inhibition	Adavosertib[a]	I
ATR kinase inhibition	Ceralasertib (AZD6738)	I-II
AURKB inhibition	AZD2811 nanoparticle	I
VEGFR tyrosine kinase inhibition	Cediranib	II
BRD4 inhibition	AZD5153	I
ATM kinase inhibition	AZD1390	I
PD-1/CTLA-4 bispecific mAb	MEDI5752	I
Anti-HER2 ADC	Trastuzumab deruxtecan (DS-8201a)	I
BCL2/BCL-XL inhibition	AZD0466	I
IL12 mRNA inhibition	MEDI1191	I
NDV GM-CSF	MEDI5395	I

[a]Previously known as AZD1775, in-licensed from Merck & Co., Inc. (MSD).

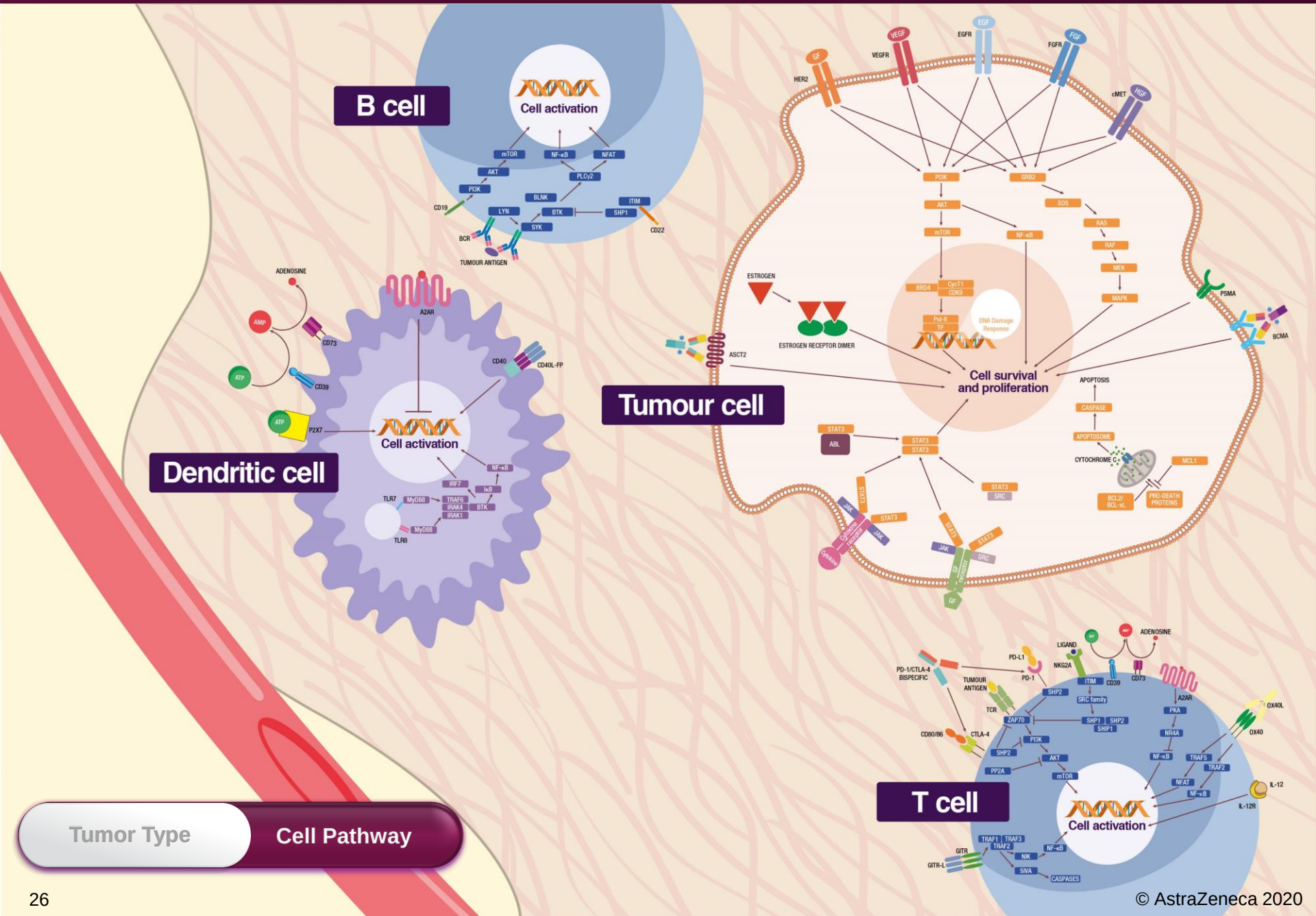


Hematologic

Investigational Molecules

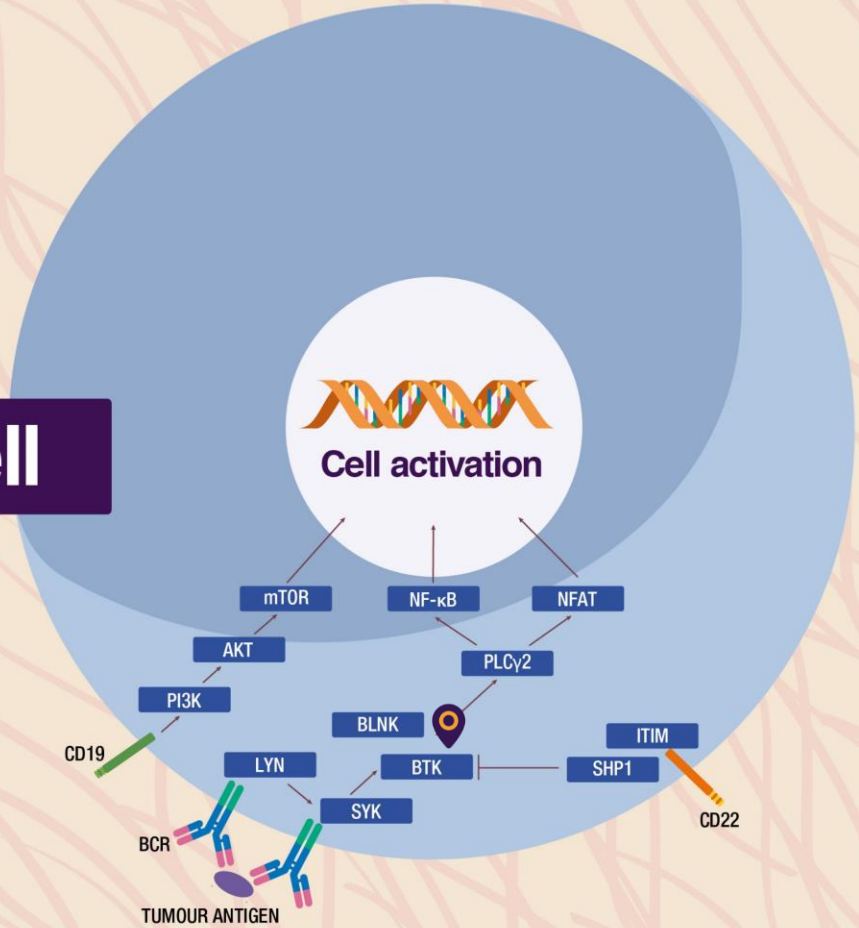
Mechanism	Compound	Phase
PD-L1 inhibition	Durvalumab	I
ATR kinase inhibition	Ceralasertib	I
BTK inhibition	Acalabrutinib[a]	I-III
MCL1 inhibition	AZD5991	I
CDK9 inhibition	AZD4573	I
Anti-BCMA	MEDI2228	I
BCL2/BCL-XL inhibition	AZD0466	I
BRD4 inhibition	AZD5153	I
AURKB inhibition	AZD2811 nanoparticle	I-II
BTK inhibition	Acalabrutinib	I

[a]Being developed in collaboration with Acerta Pharmaceuticals.

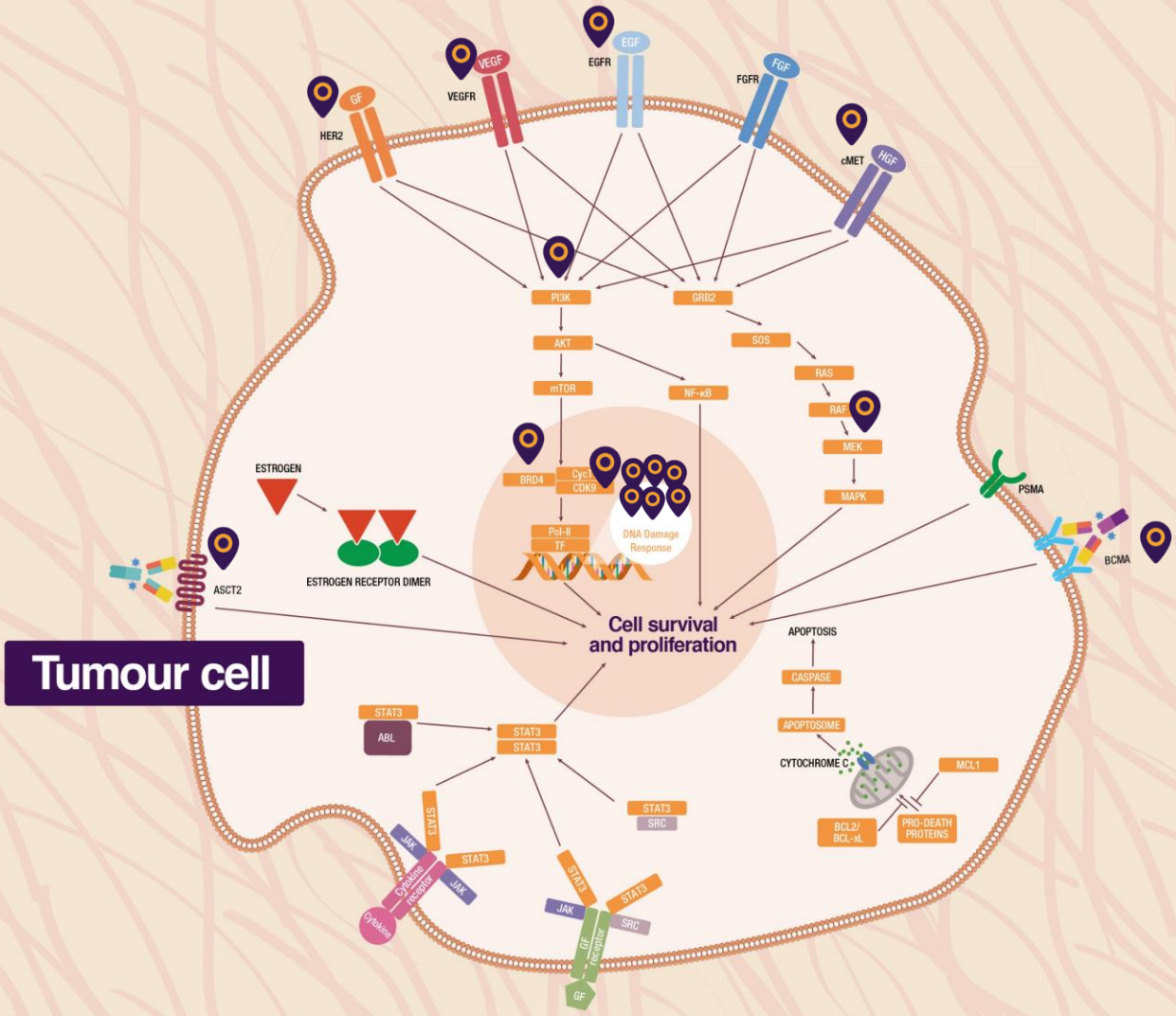


Tumor Type | Cell Pathway

B cell

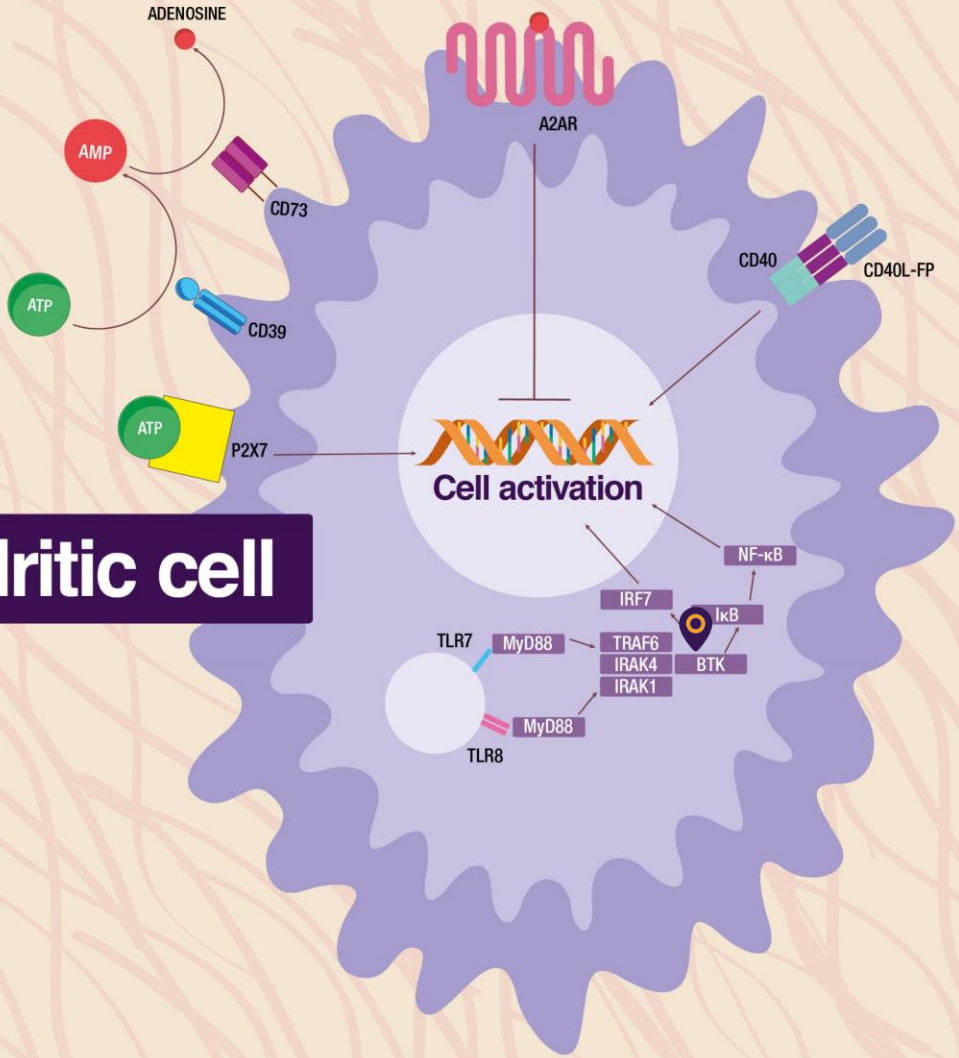


Cell Pathway

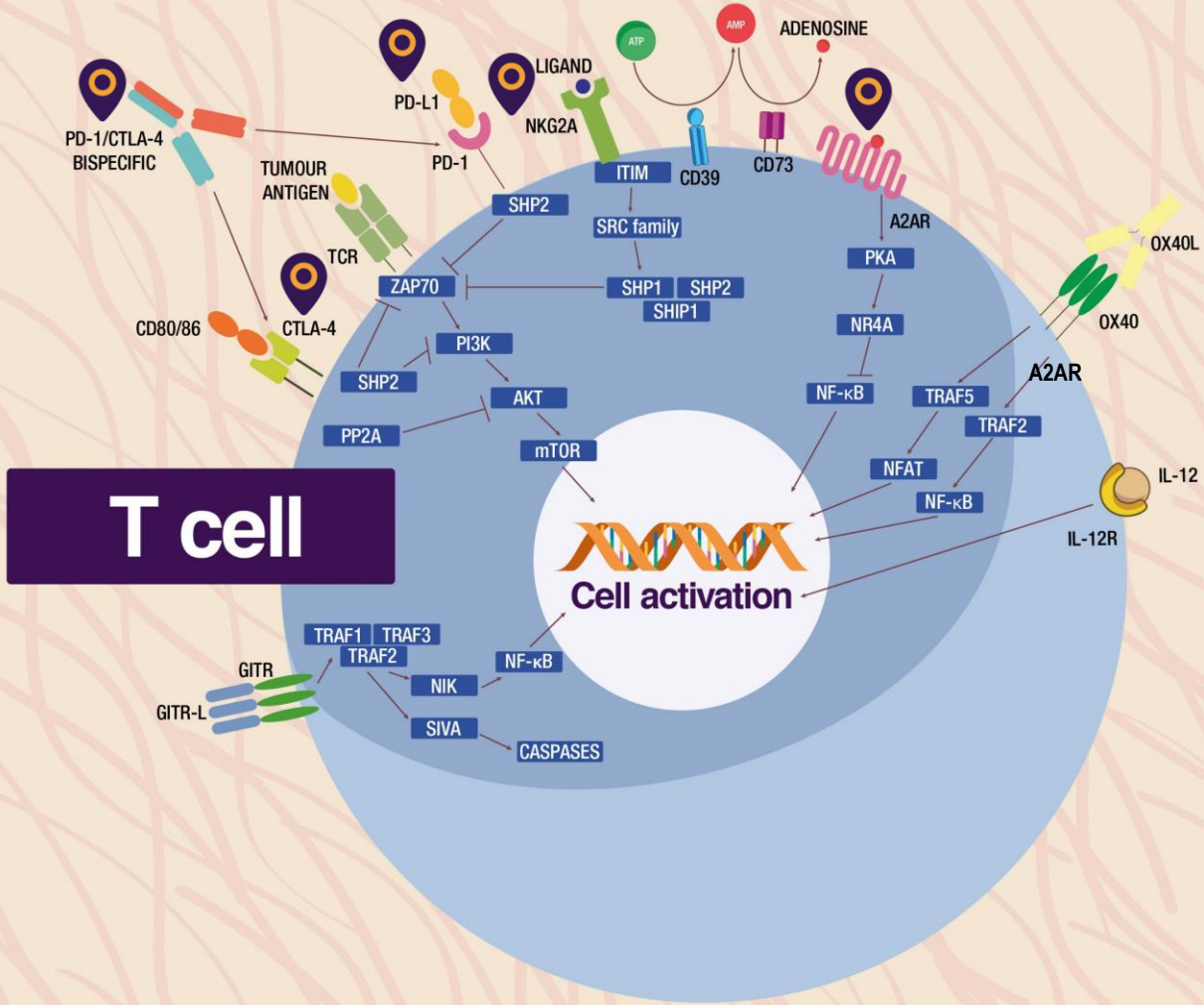


Cell Pathway

Dendritic cell



Cell Pathway



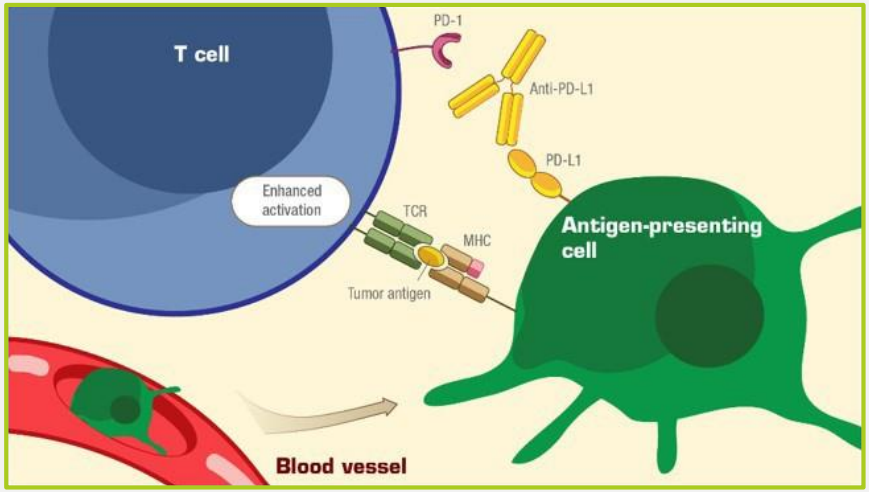
Cell Pathway

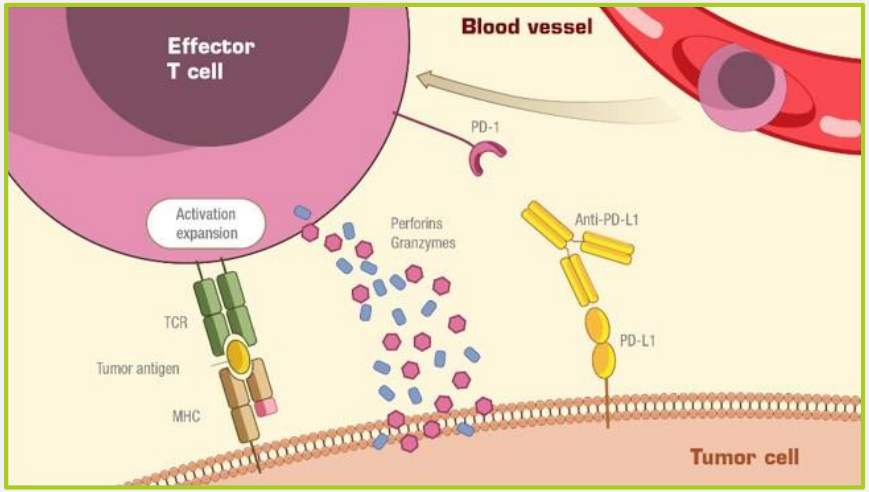
PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

PD-L1 is a cell-surface protein that binds to the receptors PD-1 and CD80 on activated T cells, B cells, and other myeloid cells. PD-L1 binding to PD-1 on activated T cells has been found to interfere with T-cell proliferation and to inhibit immune responses.1 Overexpression of PD-L1 on cancer cells and solid tumors may allow these cells to avoid immune detection and elimination.2





Figures adapted from MedImmune Oncology Pipeline: Durvalumab, targeting PD-L1. ©2013 MedImmune, LLC. 11326A. AstraZeneca; 264701, May 2013.

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Compound Overview

Durvalumab is an anti-PD-L1 mAb designed to bind PD-L1 and reduce the interaction between PD-L1 and its receptors. Durvalumab is being clinically evaluated in NSCLC, HNSCC, UC, SCLC, solid tumors, and various other cancers.

Immuno-Oncology

Activating and directing the immune system to fight cancer

Enhancing or modulating T-cell and other immune effector cell responses, strengthening antigen presentation, and reprogramming tumor-microenvironments are strategies that are being employed to promote antitumor activity against a variety of cancers.

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Clinical Trial Information

Tumor	Setting	Regimen	Phase	Trial identifier
NSCLC	Unresectable Stage III (PACIFIC 2)	Durvalumab + cCRT followed by durvalumab	III	NCT03519971
	Unresectable Stage I/II lymph node negative (PACIFIC 4)	Durvalumab following SBRT	III	NCT03833154
	Unresectable Stage III (PACIFIC 5)	Durvalumab following sCRT or concurrent CRT	III	NCT03706690
	Unresectable Stage III (PACIFIC 6)	Durvalumab following sequential CRT	II	NCT03693300
	Unresectable Stage III NSCLC (COAST)	Durvalumab following CRT ± oleclumab or monalizumab	II	NCT03822351
	Resectable Stage I-III NSCLC (NeoCOAST), neo-adjuvant	Neoadjuvant durvalumab ± oleclumab or danvatirsen or monalizumab	II	NCT03794544
	Unresectable Stage III (DUART)	Durvalumab following RT	II	NCT04249362
	Resectable Stage IIA/Select IIIB NSCLC (AEGEAN), neo-adjuvant and adjuvant	Neoadjuvant durvalumab + platinum doublet CT	III	NCT03800134
	Completely resected Stage Ib-IIIa NSCLC (BR.31), adjuvant	Durvalumab after surgery and adjuvant therapy	III	NCT02273375[a]
	Completely resected Stage II-III NSCLC (MERMAID-1)	Durvalumab + SoC chemotherapy	III	NCT04385368

[a]Externally sponsored research trial conducted by Canadian Cancer Trials Group (CCTG).

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Clinical Trial Information

Tumor	Setting	Regimen	Phase	Trial identifier
NSCLC	Metastatic (POSEIDON), 1L	Durvalumab ± tremelimumab + platinum-based CT	III	NCT03164616
	Metastatic (PEARL), 1L	Durvalumab	III	NCT03003962
	Metastatic NSCLC (MAGELLAN)	Durvalumab + oleclumab or danvatirsen or chemotherapy Durvalumab + chemotherapy + danvatirsen or oleclumab	I	NCT03819465
	Stage IV tumors that lack EGFR mutations and ALK fusions (ORION)	Durvalumab ± olaparib	II	NCT03775486
	Metastatic NSCLC in patients who progressed on anti-PD-1/PD-L1–containing therapy (HUDSON)	Durvalumab + olaparib or danvatirsen or ceralasertib or oleclumab or cediranib or trastuzumab deruxtecan	II	NCT03334617
	Locally advanced or metastatic (ARCTIC), 3L+	Durvalumab, tremelimumab, durvalumab + tremelimumab	III	NCT02352948
	Advanced NSCLC in patients who progressed on 1L osimertinib therapy (ORCHARD)	Durvalumab + carboplatin + pemetrexed, osimertinib ± savolitinib or gefitinib or necitumumab	II	NCT03944772

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Clinical Trial Information

Tumor	Setting	Regimen	Phase	Trial identifier
SCLC	Extensive-stage (CASPIAN), 1L	Durvalumab ± tremelimumab + platinum-based CT	III	NCT03043872
	Platinum-refractory extensive stage (BALTIC)	Durvalumab + tremelimumab, adavosertib + carboplatin, ceralasertib + olaparib	II	NCT02937818
	Limited stage SCLC (ADRIATIC)	Durvalumab, durvalumab + tremelimumab following concurrent CRT	III	NCT03703297
Hepatocellular (HCC)	Unresectable HCC, 1L (HIMALAYA)	Durvalumab ± tremelimumab	III	NCT03298451
	Loco-regional HCC (EMERALD-1)	Durvalumab ± bevacizumab ± transarterial chemoembolization	III	NCT03778957
	Adjuvant HCC (EMERALD-2)	Durvalumab ± bevacizumab	III	NCT03847428
	Advanced HCC (Study 22)	Durvalumab, tremelimumab, durvalumab + tremelimumab, durvalumab + bevacizumab	II	NCT02519348

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Clinical Trial Information

Tumor	Setting	Regimen	Phase	Trial identifier
Bladder	Muscle invasive bladder cancer (NIAGARA)	Durvalumab + gemcitabine + cisplatin	III	NCT03732677
	Muscle invasive bladder cancer (BISCAY)	Durvalumab ± other agents (modules A-G)	I	NCT02546661
	Urothelial carcinoma, 1L (DANUBE)	Durvalumab ± tremelimumab	III	NCT02516241
	Urinary bladder neoplasms, cisplatin-ineligible (BAYOU)	Durvalumab ± olaparib	II	NCT03459846
	Urothelial carcinoma, unresectable locally advanced or metastatic (NILE)	Durvalumab ± tremelimumab + SoC	III	NCT03682068
	Urothelial Carcinoma, BCG-naïve NMIBC (POTOMAC)	Durvalumab + BCG	III	NCT03528694
HNSCC	Metastatic HNSCC (SCORES), advanced solid tumors, 2L	Durvalumab ± danvatirsen, AZD5069 ± durvalumab, danvatirsen + durvalumab + tremelimumab, AZD5069 + durvalumab + tremelimumab	Ib/II	NCT02499328
	Recurrent/metastatic (HAWK), 2L PD-L1+	Durvalumab	II	NCT02207530
	Recurrent/metastatic (CONDOR), 2L PD-L1-	Durvalumab, tremelimumab, durvalumab + tremelimumab	II	NCT02319044
	Recurrent/metastatic (KESTREL), 1L	Durvalumab ± tremelimumab	III	NCT02551159

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Tumor	Setting	Regimen	Phase	Trial identifier
Colorectal	Metastatic microsatellite-stable colorectal cancer (MSS-CRC) , COLUMBIA-1	Durvalumab + FOLFOX + bevacizumab + oleclumab FOLFOX + bevacizumab	I/II	NCT04068610
Pancreatic	Metastatic pancreatic cancer	Durvalumab ± oleclumab + CT	I/II	NCT03611556
Advanced	Advanced solid tumors (STRONG)	Durvalumab ± tremelimumab	III	NCT03084471
	Advanced solid tumors (IND.226)	Durvalumab ± tremelimumab + SoC	I	NCT02537418[a]
	Advanced solid tumors (MEDIOLA)	Durvalumab + olaparib ± bevacizumab	I/II	NCT02734004
	Advanced solid tumors (CLOVER)	Durvalumab ± tremelimumab + CRT	I	NCT03509012
	Advanced solid tumors	MEDI5395 + durvalumab	I	NCT03889275
	Advanced solid tumors	Durvalumab ± oleclumab ± IPH5201	I	NCT04261075
Hematologic	Hematologic cancers[b]	Durvalumab ± tremelimumab	I/II	NCT03837899

[a]Externally sponsored research trial conducted by Canadian Cancer Trials Group (CCTG); [b]This study is in pediatric patients.

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Tumor	Setting	Regimen	Phase	Trial identifier
TNBC	Metastatic TNBC (BEGONIA)	Durvalumab + paclitaxel ± (oleclumab or capivasertib) or durvalumab+trastuzumab deruxtecan	I/II	NCT03742102
Ovarian	Advanced ovarian cancer (DUO-O)	CT+ bevacizumab + followed by maintenance durvalumab, bevacizumab and olaparib	III	NCT03737643
Prostate	Prostate cancer (mCRPC)	Durvalumab + AZD4635 AZD4635 + oleclumab	II	NCT04089553
Cervical	Locally advanced cervical cancer (CALLA)	Durvalumab ± SoC followed by durvalumab monotherapy	III	NCT03830866
BTC	Advanced biliary tract cancer, 1L (TOPAZ-1)	Durvalumab ± cisplatin + gemcitabine	III	NCT03875235
Endometrial	Advanced and recurrent endometrial cancer (DUO-E)	Durvalumab ± olaparib	III	NCT04269200

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

References

Sznol M, Chen L. Clin Cancer Res. 2013;19(5):1021-1034.
Creelan BC. Cancer Control. 2014;21(1):80-89.

PD-L1 inhibition

Durvalumab

Tumor Types: NSCLC, SCLC, HCC, Bladder, HNSCC Colorectal, Pancreatic, Advanced Solid Tumors, Hematologic malignancies, TNBC, Ovarian, Endometrial, Prostate, Cervical, and BTC

Abbreviations

View all abbreviations & acronyms

1L/2L	First line/Second line
BCG	Bacille Calmette-Guerin (biologic)
BTC	Biliary tract cancer
CT	Chemotherapy
CD80	Cluster of differentiation 80
mCRPC	Metastatic castration-resistant prostate cancer
HNSCC	Head and neck squamous cell carcinoma
mAb	Monoclonal antibody
UC	Urothelial carcinoma
TNBC	Triple negative breast cancer
SCRT	Short course radiation therapy
SBRT	Stereotactic body radiation therapy
ALK	Anaplastic lymphoma kinase
MHC	Major histocompatibility complex
HCC	Hepatocellular carcinoma
MSS-CRC	Microsatellite-stable colorectal cancer
NSCLC	Non-small-cell lung cancer
PD-1	Programmed cell death-1
PD-L1	Programmed cell death ligand-1
TCR	T-cell receptor
SCLC	Small-cell lung cancer
CRT	Chemoradiotherapy
SoC	Standard of care

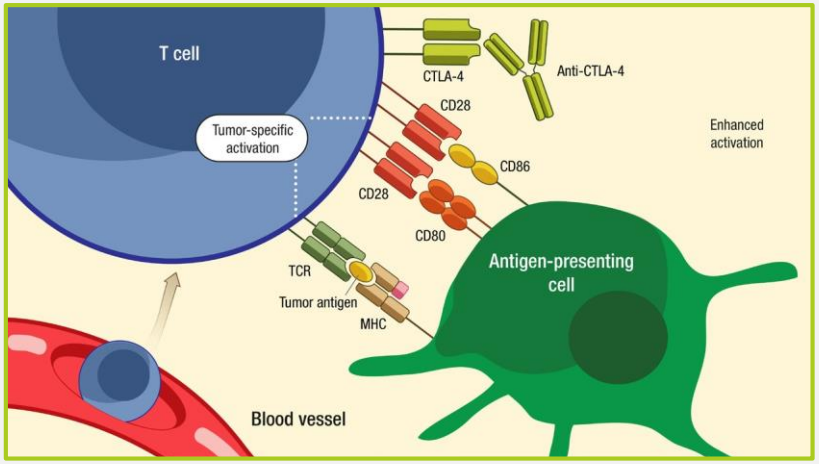
CTLA-4 inhibition

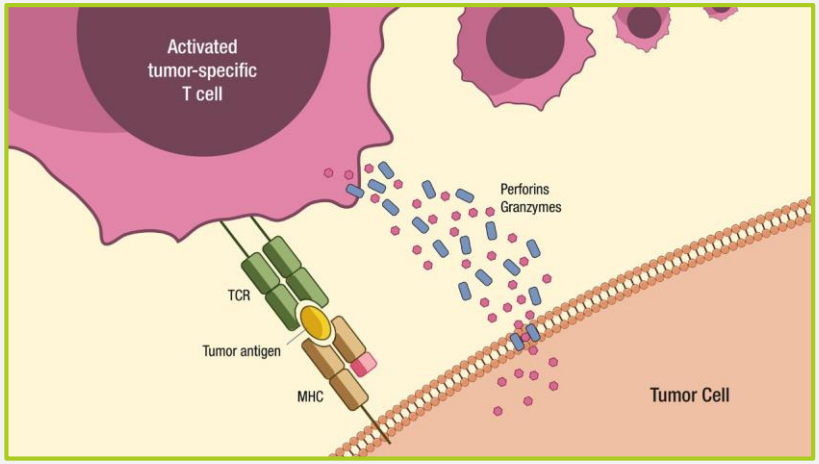
Tremelimumab

Tumor Types: Advanced solid tumors

Target Overview

CTLA-4 is expressed exclusively on the surface of T cells.1 CTLA-4 serves to inhibit T-cell activation through delivery of inhibitory signals and through ligand competition with the costimulatory receptor, CD28.1,2
Inhibition of CTLA-4 can shift the balance of signaling in the immune system in favor of greater T-cell activation, engendering a greater immune response and potentially resulting in the rejection of tumor by the host's immune system.2





Figures adapted from MedImmune Oncology Pipeline: Tremelimumab, targeting CTLA-4. ©2013 MedImmune, LLC. 11326A.
AstraZeneca; 264701, May 2013.

CTLA-4 inhibition

Tremelimumab

Tumor Types: Advanced solid tumors

Compound Overview

Tremelimumab is an investigational anti-CTLA-4 mAb that is being clinically evaluated in combination with durvalumab (a PD-L1 inhibitor) for the potential treatment of cancer.

Immuno-Oncology

Activating and directing the immune system to fight cancer

Enhancing or modulating T-cell and other immune effector cell responses, strengthening antigen presentation, and reprogramming tumor-microenvironments are strategies that are being employed to promote antitumor activity against a variety of cancers.

CTLA-4 inhibition

Tremelimumab

Tumor Types: Advanced solid tumors

Clinical Trial Information[a]

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	Tremelimumab ± durvalumab	II	NCT02527434

[a]For information on clinical trials of tremelimumab in combination with durvalumab, please refer to the PD-L1 section of this brochure.

CTLA-4 inhibition

Tremelimumab

Tumor Types: Advanced solid tumors

References

1. Pardoll DM. *Nat Rev Cancer*. 2012;12(4):252-264.
2. Wolchok JD, Saenger Y. *Oncologist*. 2008;13(suppl 4):2-9.

CTLA-4 inhibition

Tremelimumab

Tumor Types: Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

CD28	Cluster of differentiation 28
CD80/86	Cluster of differentiation 80/86
CTLA-4	Cytotoxic T-lymphocyte-associated antigen-4
mAb	Monoclonal antibody
MHC	Major histocompatibility complex
TCR	T-cell receptor
PD-L1	Programmed cell death ligand-1

PD-1/CTLA-4 bispecific mAb

MEDI5752

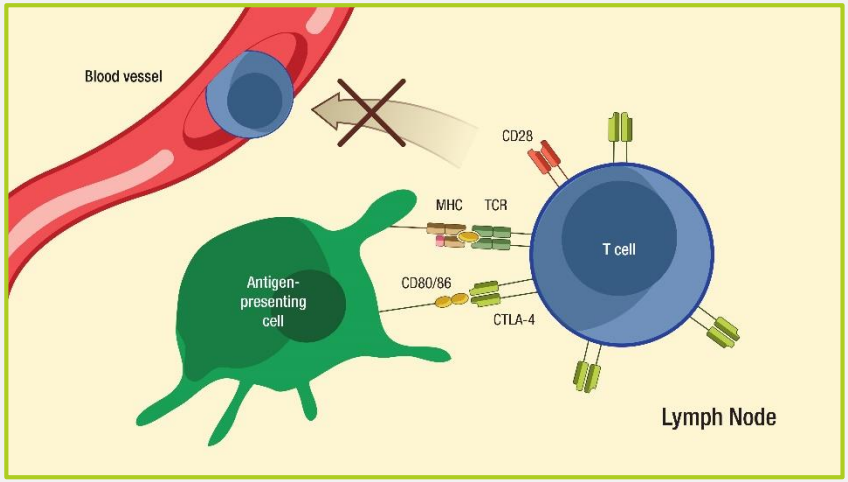
Tumor Types: Advanced solid tumors

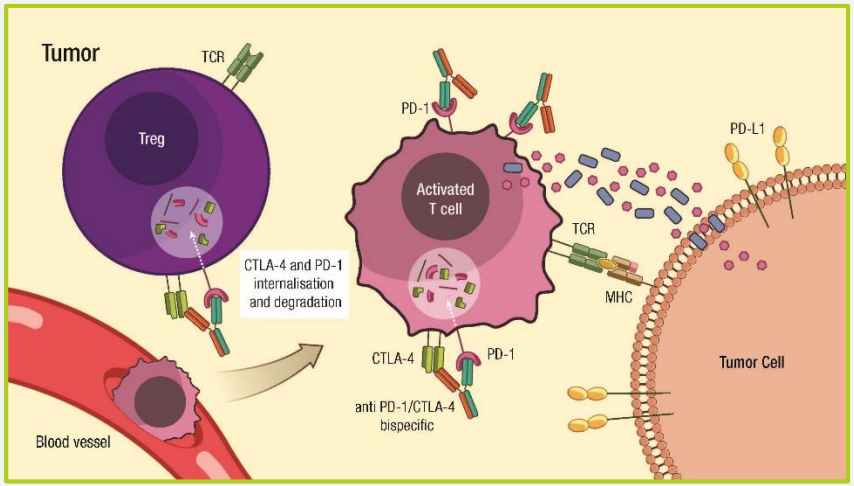
Target Overview

PD-1 is a cell surface receptor that interacts with 2 ligands, PD-L1 and PD-L2, to deliver inhibitory signals to T cells, limiting their function.[1]

CTLA-4 is expressed exclusively on the surface of effector and regulatory T cells.[1] CTLA-4 serves to inhibit T-cell activation through ligand competition with the costimulatory receptor, CD28.[1]

Blockade of PD-1 and CTLA-4 may potentiate antitumor immunity.[2]





PD-1/CTLA-4 bispecific mAb

MEDI5752

Tumor Types: Advanced solid tumors

Compound Overview

MEDI5752 is an investigational monovalent bispecific humanized IgG1 mAb binding to PD-1 and CTLA-4 receptors. It is designed to fully suppress the PD-1 pathway and leads to downregulation and degradation of the PD-1 receptor.

MEDI5752 preferentially inhibits CTLA-4 on activated T cells versus peripheral T cells, uncoupling CTLA-4-dependent peripheral toxicity from antitumor activity.

MEDI5752 is currently being clinically evaluated in the treatment of advanced solid tumors.

Immuno-Oncology

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PD-1/CTLA-4 bispecific mAb

MEDI5752

Tumor Types: Advanced solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	MEDI5752	II	NCT03530397

PD-1/CTLA-4 bispecific mAb

MEDI5752

Tumor Types: Advanced solid tumors

References

1. Pardoll DM. *Nat Rev Cancer*. 2012;12(4):252-264.
2. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. *N Engl J Med.* 2015;373(1):23-34.

PD-1/CTLA-4 bispecific mAb

MEDI5752

Tumor Types: Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

CD28	Cluster of differentiation 28	**PD-1**	Programmed cell death-1
CD80/86	Cluster of differentiation 80/86	**PD-L1**	Programmed cell death ligand-1
CTLA-4	Cytotoxic T-lymphocyte-associated antigen-4	**PD-L2**	Programmed cell death ligand-2
MHC	Major histocompatibility complex	**TCR**	T-cell receptor
mAB	Monoclonal antibody	**Treg**	Regulatory T cell

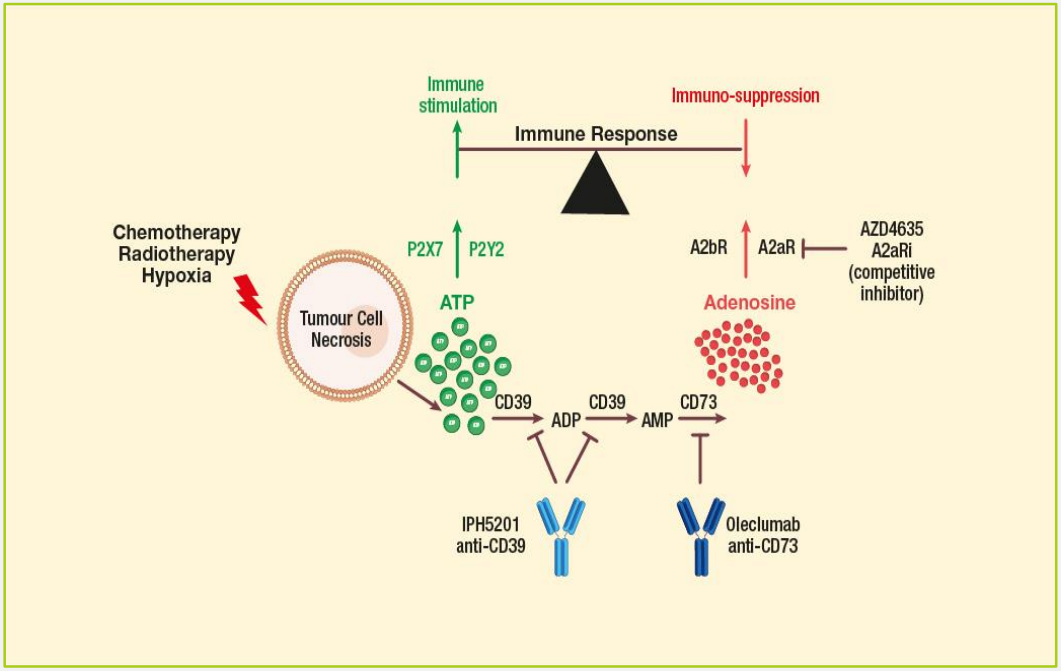
A2AR antagonism

AZD4635

Tumor Types: Solid tumors and Prostate cancer

Target Overview

Elevated extracellular levels of adenosine in the microenvironment of many solid tumors, driven by overexpression of CD73 (an ectoenzyme that catalyzes the conversion of AMP to adenosine) and by tissue breakdown and hypoxia, can exert potent immunosuppressive effects by binding of adenosine to the A2AR on antigen-presenting cells and lymphocytes, including T cells. This is known to suppress many aspects of antitumor immunity, including T-cell effector function.[1,2]



A2AR antagonism

AZD4635

Tumor Types: Solid tumors and Prostate cancer

Compound Overview

AZD4635 is currently being clinically evaluated as a monotherapy and in combination with durvalumab (anti-PD-L1) in various solid tumor malignancies. AZD4635 is also being studied in combination with durvalumab or oleclumab (anti-CD73) in prostate cancer.

Immuno-Oncology

Activating and directing the immune system to fight cancer

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A2AR antagonism

AZD4635

Tumor Types: Solid tumors and Prostate cancer

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	AZD4635 ± durvalumab	I	NCT02740985
Prostate cancer	AZD4635 + durvalumab AZD4635 + oleclumab	II	NCT04089553
Advanced solid tumors (Japan)	AZD4635	I	NCT03980821

A2AR antagonism

AZD4635

Tumor Types: Solid tumors and Prostate cancer

References

1. Vijayan D, Young A, Teng MWL, et al. *Nat Rev Cancer*. 2017;17(12):709-724.
2. Vigano S, Alatzoglou D, Irving M, et al. *Front Immunol*. 2019;10:925.

A2AR antagonism

AZD4635

Tumor Types: Solid tumors and Prostate cancer

Abbreviations

View all abbreviations & acronyms

A2ARI	Adenosine 2A receptor inhibitor
A2AR	Adenosine 2A receptor
AMP	Adenosine monophosphate
ATP	Adenosine triphosphate
CD39	Cluster of differentiation 39
P2Y2	P2Y purinoreceptor 2
P2X7	P2X purinoreceptor 7
A2BR	Adenosine 2B receptor
CD73	Cluster of differentiation 73
ADP	Adenosine diphosphate
NSCLC	Non-small-cell lung cancer
EGFRm	Epidermal growth factor receptor mutation
PD-L1	Programmed cell death ligand-1

CD73 inhibition

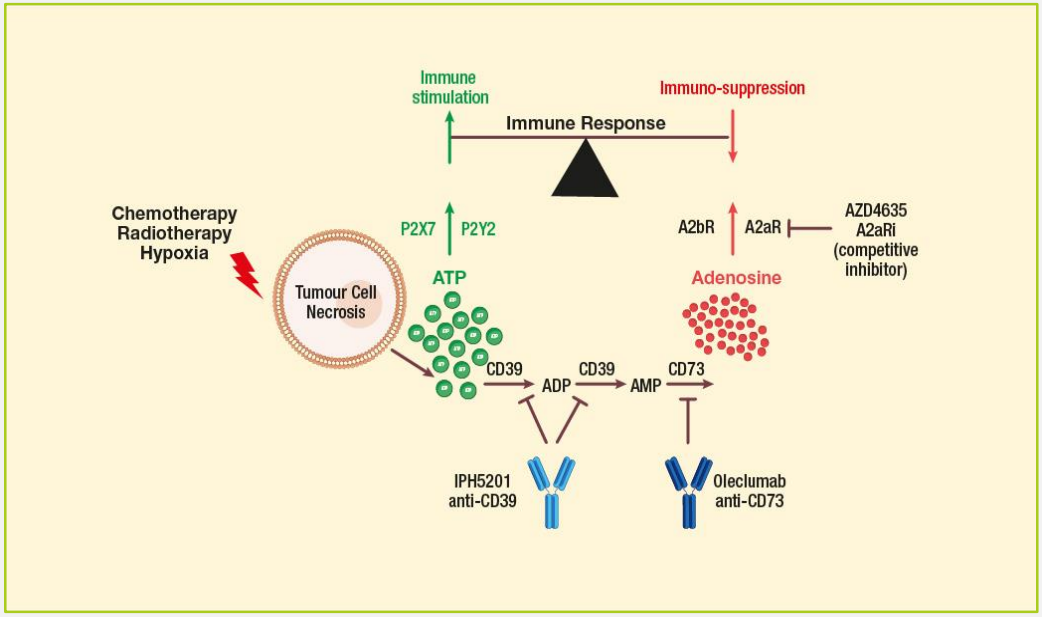
Oleclumab (MEDI9447)

Tumor Types: Solid tumors, Prostate, Colorectal, Breast, NSCLC, and Pancreatic cancer

Target Overview

CD73, or ecto-5'-nucleotidase, is a cell surface enzyme expressed on tumor cells, endothelial cells, lymphoid cells, and myeloid cells, including antigen presenting cells.[1] It catalyzes the conversion of extracellular AMP to the nucleoside adenosine.[1,2]

Overexpression of CD73 and elevated extracellular levels of adenosine in the microenvironments of many solid tumors are known to exert potent immunosuppressive effects by binding of adenosine to adenosine receptors on antigen-presenting cells and lymphocytes, including T cells.[1,2] This is known to suppress many aspects of antitumor immunity.



CD73 inhibition

Oleclumab (MEDI9447)

Tumor Types: Solid tumors, Prostate, Colorectal, Breast, NSCLC, and Pancreatic cancer

Compound Overview

Oleclumab is an investigational human IgG1λ monoclonal antibody that selectively binds to and inhibits the ectonucleotidase activity of CD73. Results from preclinical studies suggest that oleclumab may help to overcome adenosine-mediated immunosuppression in a number of solid tumor model systems. The molecule is currently being clinically evaluated in solid tumor malignancies.

Immuno-Oncology

Activating and directing the immune system to fight cancer

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CD73 inhibition

Oleclumab (MEDI9447)

Tumor Types: Solid tumors, Prostate, Colorectal, Breast, NSCLC, and Pancreatic cancer

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	Oleclumab ± durvalumab	I	NCT02503774
Metastatic NSCLC in patients who progressed on an anti-PD-1/PD-L1–containing therapy (HUDSON)	Durvalumab + olaparib or danvatirsen or ceralasertib or oleclumab or cediranib or trastuzumab deruxtecan	II	NCT03334617
Advanced pancreatic cancer	Oleclumab + chemotherapy combination ± durvalumab	I/II	NCT03611556
Metastatic TNBC (BEGONIA)	Oleclumab or capivasertib or durvalumab + paclitaxel or trastuzumab deruxtecan	I/II	NCT03742102
Unresectable Stage III NSCLC (COAST)	Durvalumab ± oleclumab or monalizumab	II	NCT03822351
Resectable Stage I-IIIa NSCLC (NeoCOAST)	Durvalumab ± oleclumab or monalizumab or danvatirsen	II	NCT03794544

CD73 inhibition

Oleclumab (MEDI9447)

Tumor Types: Solid tumors, Prostate, Colorectal, Breast, NSCLC, and Pancreatic cancer

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumor	Oleclumab ± IPH5201 ± durvalumab	I	NCT04261075
Prostate cancer	AZD4635 + oleclumab AZD4635 + durvalumab	II	NCT04089553
Metastatic NSCLC (MAGELLAN)	Durvalumab + oleclumab or danvatirsen or chemotherapy Durvalumab + chemotherapy + danvatirsen or oleclumab	I	NCT03819465
Metastatic microsatellite-stable colorectal cancer (COLUMBIA-1)	FOLFOX + bevacizumab, FOLFOX + bevacizumab + durvalumab + oleclumab	I/II	NCT04068610
Advanced solid malignancies	AZD4635 + durvalumab or oleclumab or enzalutamide or abiraterone acetate or chemotherapy AZD4635 + durvalumab + oleclumab	I	NCT02740985

CD73 inhibition

Oleclumab (MEDI9447)

Tumor Types: Solid tumors, Prostate, Colorectal, Breast, NSCLC, and Pancreatic cancer

References

1. Vijayan D, Young A, Teng MWL, et al. *Nat Rev Cancer*. 2017;17(12):709-724.
2. Vigano S, Alatzoglou D, Irving M, et al. *Front Immunol*. 2019;10:925.

CD73 inhibition

Oleclumab (MEDI9447)

Tumor Types: Solid tumors, Prostate, Colorectal, Breast, NSCLC, and Pancreatic cancer

Abbreviations

View all abbreviations & acronyms

A2AR	Adenosine 2A receptor
A2BR	Adenosine 2B receptor
A2ARI	Adenosine 2A receptor inhibitor
AMP	Adenosine monophosphate
ATP	Adenosine triphosphate
PD-L1	Programmed cell death ligand-1
P2Y2	P2Y purinoreceptor 2
P2X7	P2X purinoreceptor 7
CD73	Cluster of differentiation 73
ADP	Adenosine diphosphate
TNBC	Triple negative breast cancer
NSCLC	Non-small-cell lung cancer
EGFRm	Epidermal growth factor receptor mutation
PD-1	Programmed cell death-1
IgG	Immunoglobulin G

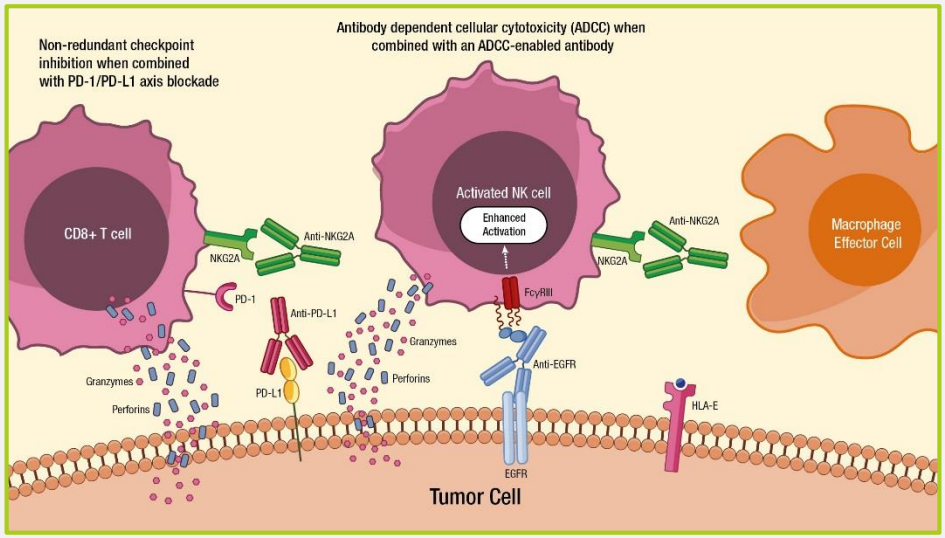
NKG2A inhibition

Monalizumab

Tumor Types: Advanced solid tumors, NSCLC, HNSCC, and CRC

Target Overview

NKG2A is an immune checkpoint inhibitor receptor that is expressed on NK cells, as well as tumor infiltrating CD8+ T cells.[1,2] Its natural ligand, HLA-E, is highly expressed on many solid and hematologic tumors.[3,4] Binding of tumor-associated HLA-E to NKG2A inhibits NK cell and CD8+ T-cell activation and ablates NK cell and CD8+ T-cell–mediated antitumor killing.[5,6]



NKG2A inhibition

Monalizumab

Tumor Types: Advanced solid tumors, NSCLC, HNSCC, and CRC

Compound Overview

Monalizumab[a] is an investigational anti-NKG2A antibody that binds to NKG2A on NK cells and intratumoral CD8+ T cells and helps block the inhibitory interactions between tumor-associated HLA-E and the NKG2A receptor. This, in turn, may enhance innate immune antitumor responses. This molecule is being clinically evaluated in various solid tumors.

[a]AstraZeneca has a co-development agreement with Innate Pharma to develop monalizumab in oncology.

Some compounds illustrated from AstraZeneca may refer to selected pipeline products still under investigation and development. AstraZeneca pipeline products are investigational products and, as such, are not approved by the US Food & Drug Administration (FDA), the European Medicines Agency (EMA), or any other regulatory agency for the uses under investigation. Information regarding these investigational products should under no circumstances be regarded as a recommendation for their use or of their safety or efficacy.

Immuno-Oncology

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NKG2A inhibition

Monalizumab

Tumor Types: Advanced solid tumors, NSCLC, HNSCC, and CRC

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	Monalizumab + durvalumab ± cetuximab	I/II	NCT02671435
Unresectable Stage III NSCLC (COAST)	Durvalumab ± oleclumab or monalizumab	II	NCT03822351
Resectable Stage III NSCLC (NeoCOAST)	Durvalumab ± oleclumab or monalizumab or danvatirsen	II	NCT03794544
Recurrent or metastatic HNSCC	Monalizumab + cetuximab ± anti-PD-L1	I/II	NCT02643550

NKG2A inhibition

Monalizumab

Tumor Types: Advanced solid tumors, NSCLC, HNSCC, and CRC

References

1. Platonova S, Cherfils-Vicini J, Damotte D, et al. *Cancer Res*. 2011;71(16):5412-5422.
2. Sheu BC, Chiou SH, Lin HH, et al. *Cancer Res*. 2005;65(7):2921-2929.
3. Braud VM, Allan DS, O'Callaghan CA, et al. *Nature*. 1998;391(6669):795-799.
4. Talebian Yazdi M, van Riet S, van Schadewijk A, et al. *Oncotarget*. 2016;7(3):3477-3488.
5. Pace E, Di Sano C, Ferraro M, et al. *Eur J Cancer*. 2011;47(2):296-304.
6. Speiser DE, Pittet MJ, Valmori D, et al. *J Exp Med*. 1999;190(6):775-782.

NKG2A inhibition

Monalizumab

Tumor Types: Advanced solid tumors, NSCLC, HNSCC, and CRC

Abbreviations

View all abbreviations & acronyms

CD8	Cluster of differentiation 8	**NK**	Natural killer
ADCC	Antibody-dependent cellular cytotoxicity	**NKG2A**	Natural killer cell lectin-like receptor
HNSCC	Head and neck squamous cell carcinoma	**CRC**	Colorectal cancer
HLA-E	HLA class I histocompatibility antigen E	**PD-1**	Programmed cell death-1
NSCLC	Non-small-cell lung cancer	**PD-L1**	Programmed cell death ligand-1

CD39 inhibition

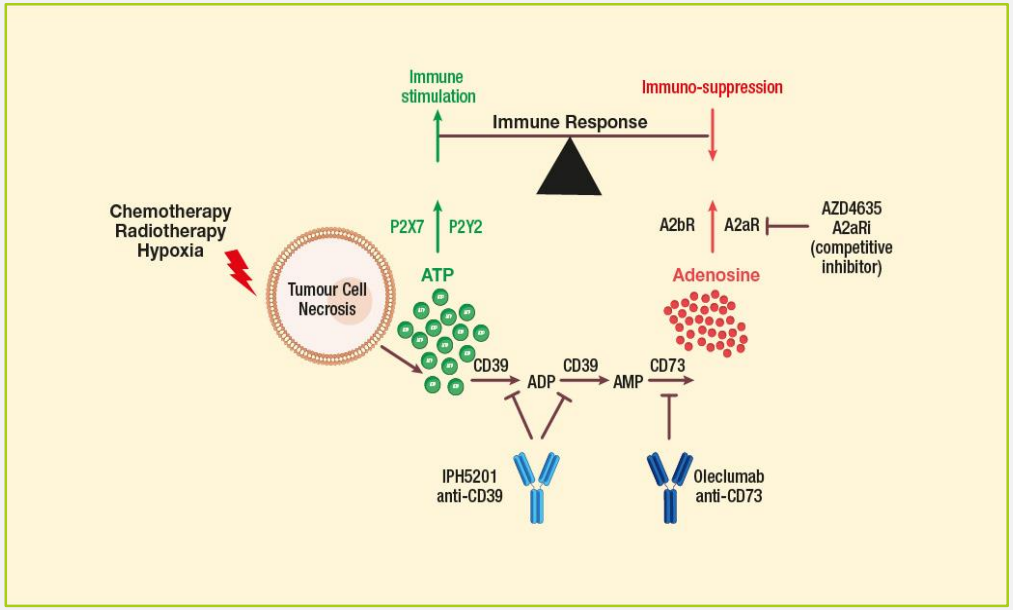
IPH5201

Tumor Types: Advanced solid tumors

Target Overview

CD39 is a cell surface enzyme expressed on stromal and immune cells in tumors that hydrolyzes immunostimulatory ATP to ADP and AMP in the extracellular space. CD73 further metabolizes AMP to immunosuppressive adenosine, which accumulates in the tumor microenvironment.[1,2]

ATP promotes activation of antigen-presenting cells, whereas adenosine exerts immunosuppressive effects on both the myeloid and lymphoid compartments.[3]



CD39 inhibition

IPH5201

Tumor Types: Advanced solid tumors

Compound Overview

IPH5201[a] is an investigational humanized IgG1 antibody that inhibits CD39-mediated hydrolysis of ATP to ADP and AMP. In preclinical models, inhibition of CD39-mediated hydrolysis of ATP promotes accumulation of immune-stimulatory ATP and reduces the formation of immunosuppressive adenosine, thereby leading to increased antitumor immunity.[4,5]

[a]Partnered asset.

Some compounds illustrated from AstraZeneca may refer to selected pipeline products still under investigation and development. AstraZeneca pipeline products are investigational products and, as such, are not approved by the US Food & Drug Administration (FDA), the European Medicines Agency (EMA), or any other regulatory agency for the uses under investigation. Information regarding these investigational products should under no circumstances be regarded as a recommendation for their use or of their safety or efficacy.

Immuno-Oncology

Activating and directing the immune system to fight cancer

Enhancing or modulating T-cell and other immune effector cell responses, strengthening antigen presentation, and reprogramming tumor-microenvironments are strategies that are being employed to promote antitumor activity against a variety of cancers.

CD39 inhibition

IPH5201

Tumor Types: Advanced solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	IPH5201 ± durvalumab ± oleclumab	I	NCT04261075

CD39 inhibition

IPH5201

Tumor Types: Advanced solid tumors

References

1. Allard B, Beavis PA, Darcy PK, et al. *Curr Opin Pharmacol*. 2016;29:7-16.
2. Allard B, Longhi MS, Robson SC, et al. *Immunol Rev*. 2017;276(1):121-144.
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4. Perrot I, Michaud HA, Giraudon-Paoli M, et al. *Cell Rep*. 2019;27(8):2411-2425.e9.
5. Li XY, Moesta AK, Xiao C, et al. *Cancer Discov*. 2019;9(12):1754-1773.

CD39 inhibition

IPH5201

Tumor Types: Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

AMP	Adenosine monophosphate	**CD39**	Cluster of differentiation 39
ADP	Adenosine diphosphate	**CD73**	Cluster of differentiation 73
ATP	Adenosine triphosphate	**IgG1**	Immunoglobulin G1
A2AR	Adenosine 2A receptor	**P2X7**	P2X purinoreceptor 7
A2BR	Adenosine 2B receptor	**A2ARI**	Adenosine 2A receptor inhibitor

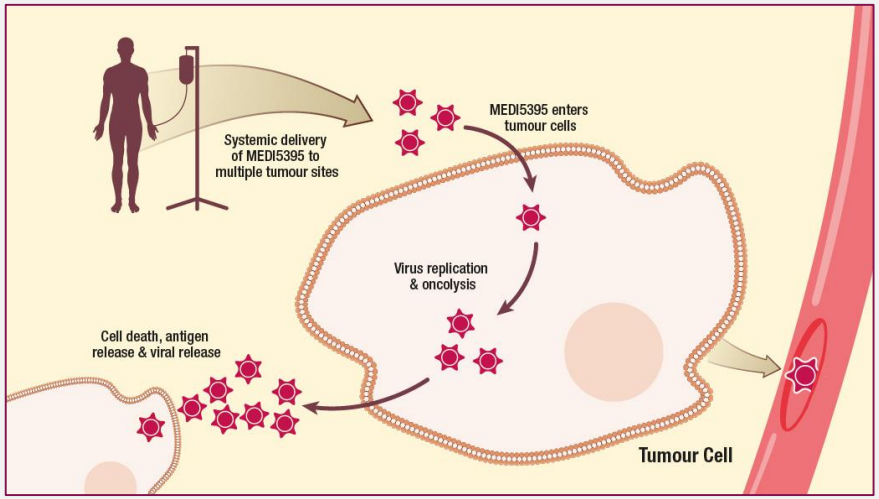
NDV GM-CSF

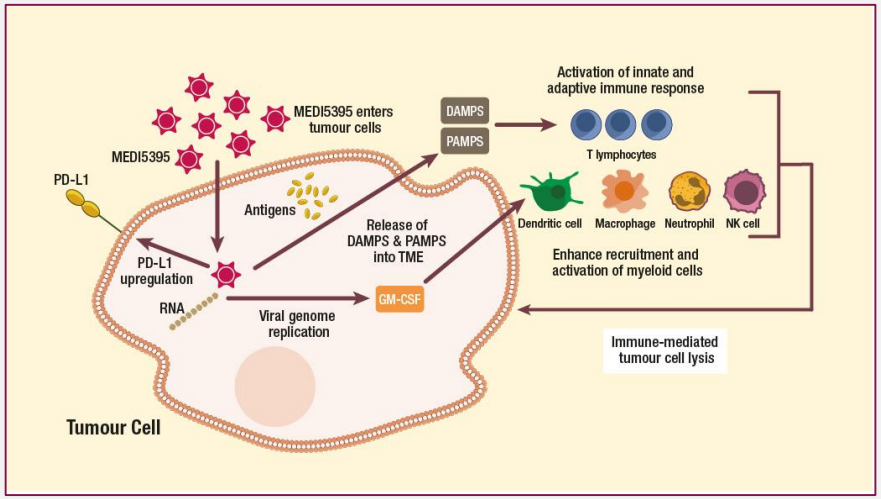
MEDI5395

Tumor Types: Advanced solid tumors

Target Overview

Newcastle Disease Virus (NDV) is an avian paramyxovirus that can selectively infect, replicate within, and kill cancer cells. NDV infection and subsequent oncolysis can lead to release of inflammatory cytokines and chemokines, upregulation of PD-L1 on surface of infected cells, reduction in immune suppressive capacity within tumor microenvironment, and induction of an adaptive antitumor immune response.[1]





NDV GM-CSF

MEDI5395

Tumor Types: Advanced solid tumors

Compound Overview

MEDI5395 is an investigational recombinant NDV engineered to express GM-CSF.[1] It is designed to selectively infect, replicate within, and kill tumor cells following systemic administration, while the virus-dependent local expression of GM-CSF within the TME could potentiate antitumor immune responses.

Immuno-Oncology

Activating and directing the immune system to fight cancer

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NDV GM-CSF

MEDI5395

Tumor Types: Advanced solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	MEDI5395 + durvalumab	I	NCT03889275

NDV GM-CSF

MEDI5395

Tumor Types: Advanced solid tumors

References

1. Cheng X, Wang W, Xu Q, et al. *J Virol.* 2016;90(11):5343-5352.

NDV GM-CSF

MEDI5395

Tumor Types: Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

GM-CSF	Granulocyte-macrophage colony-stimulating factor	**DAMPs**	Damage-associated molecular patterns
NDV	Newcastle disease virus	**PAMPs**	Pathogen-associated molecular patterns
PD-L1	Programmed cell death ligand-1	**NK**	Natural Killer
TME	Tumor microenvironment		

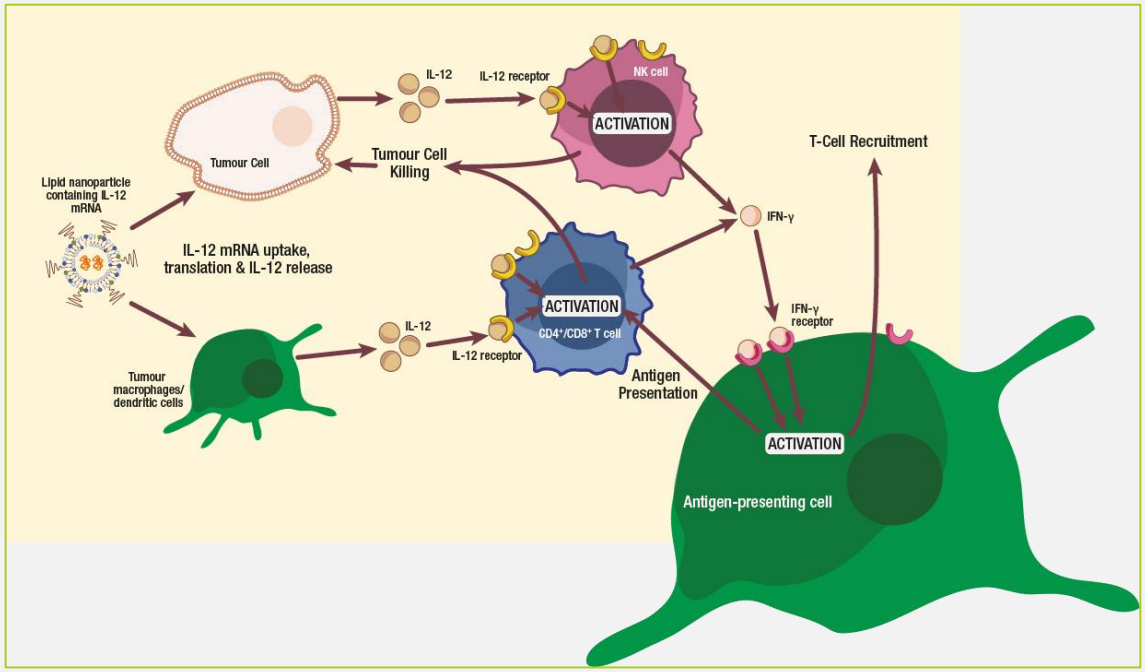
IL12 mRNA

MEDI1191

Tumor Types: Advanced solid tumors

Target Overview

As a central mediator of TH1 immune responses, IL-12 guides the differentiation of TH1 T cells, enhances activation and cytotoxic activity of NK and cytotoxic T cells, and induces expression of IFNγ by innate and adaptive immune cells.[1] IFNγ induces antigen presentation and production of T-cell chemokines and reduces myeloid immunosuppression. Overexpression of IL-12 in tumors, therefore, promotes antitumor immunity.[2]



IL12 mRNA

MEDI1191

Tumor Types: Advanced solid tumors

Compound Overview

MEDI1191 (IL-12 mRNA) is an investigational lipid nanoparticle (LNP) formulated therapy developed for intratumoral (IT) injection. IT injection of MEDI1191 is designed to drive local IL-12 production in deep-seated and superficial lesions, which will sensitize IO refractory tumors to other IO therapies, including PD-L1. MEDI1191 is being evaluated in an FIH trial in patients with advanced solid tumors.

Immuno-Oncology

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IL12 mRNA

MEDI1191

Tumor Types: Advanced solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors	A study of MEDI1191 administered in sequential and concurrent combination with durvalumab	I	NCT03946800

IL12 mRNA

MEDI1191

Tumor Types: Advanced solid tumors

References

1. Trinchieri G. *Nat Rev Immunol.* 2003;3(2):133-146.
2. Tugues S, Burkhard SH, Ohs I, et al. *Cell Death Differ.* 2015;22(2):237-246.

IL12 mRNA

MEDI1191

Tumor Types: Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

CD4	Cluster of differentiation 4	**CD8**	Cluster of differentiation 8
IL-12	Interleukin-12	**IT**	Intratumoral
mRNA	Messenger RNA	**IO**	Immuno-oncology
NK	Natural killer	**PD-L1**	Programmed cell death ligand-1
IFNγ	Interferon γ	**FIH**	First in human
LNP	Lipid nanoparticle	**TH1**	Type 1 helper

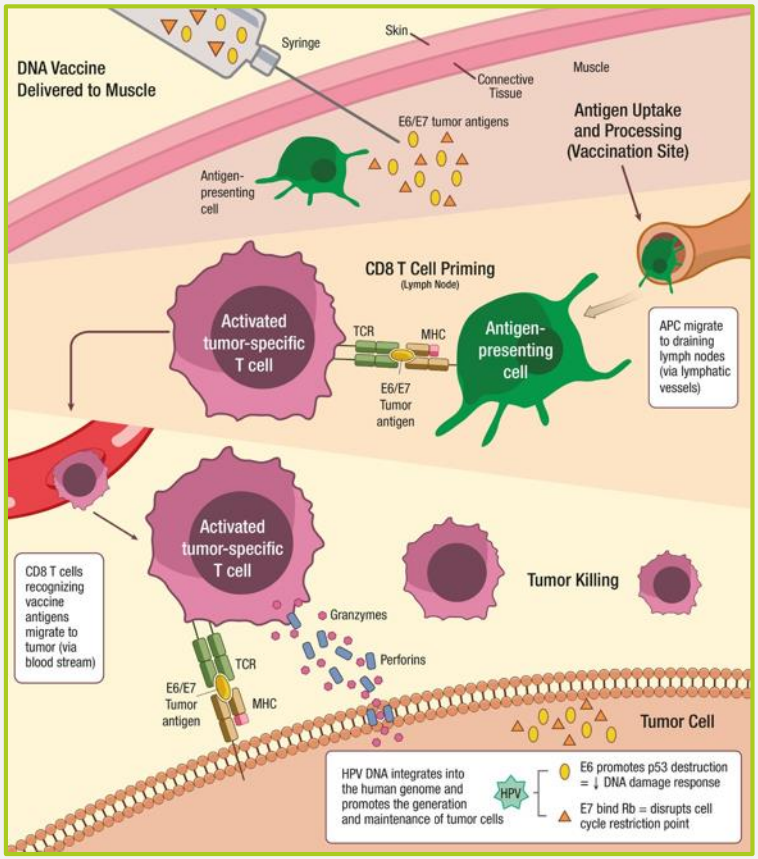
Plasmid DNA vaccine

MEDI0457

Tumor Types: HPV16/18+ HNSCC

Target Overview

Approximately 85%-90% of all HPV-associated cancers are attributable to HPV-16 or HPV-18. Viral E6 proteins regulate p53 tumor suppressors, and viral E7 proteins regulate Rb tumor suppressors.[1]



Plasmid DNA vaccine

MEDI0457

Tumor Types: HPV16/18+ HNSCC

Compound Overview

MEDI0457[a] is an investigational plasmid DNA vaccine consisting of 3 plasmids expressing HPV-16 and HPV-18 viral E6 and E7 proteins, along with IL-12 as an adjuvant. MEDI0457 is administered via intramuscular injection followed by electroporation and has been shown to generate a robust immune response in patients with HPV-driven high-grade cervical dysplasia, as well as in HPV-associated head and neck squamous cell carcinoma.[2,3]
MEDI0457 is being clinically evaluated in combination with durvalumab in various malignancies.

[a]MEDI0457 is being developed in partnership with Inovio Pharmaceuticals, Inc.

Immuno-Oncology

Activating and directing the immune system to fight cancer

Enhancing or modulating T-cell and other immune effector cell responses, strengthening antigen presentation, and reprogramming tumor-microenvironments are strategies that are being employed to promote antitumor activity against a variety of cancers.

Plasmid DNA vaccine

MEDI0457

Tumor Types: HPV16/18+ HNSCC

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
HPV16/18+ HNSCC	MEDI0457 + durvalumab	Ib/IIa	NCT03162224

Plasmid DNA vaccine

MEDI0457

Tumor Types: HPV16/18+ HNSCC

References

1. United States Cancer Statistics Data Brief. Centers for Disease Control and Prevention website. https://www.cdc.gov/cancer/hpv/statistics/cases.htm. Accessed February 4, 2020.
2. Trimble CL, Morrow MP, Kraynyak KA, et al. *Lancet.* 2015;386(10008):2078-2088.
3. Aggarwal C, Cohen RB, Morrow MP, et al. Abstract presented at: ASCO; June 2-6, 2017; Chicago, IL. Abs 6073.

Plasmid DNA vaccine

MEDI0457

Tumor Types: HPV16/18+ HNSCC

Abbreviations

View all abbreviations & acronyms

APC	Antigen-presenting cell	**HPV**	Human papillomavirus
CD8	Cluster of differentiation 8	**MHC**	Major histocompatibility complex
HNSCC	Head and neck squamous cell carcinoma	**TCR**	T-cell receptor
IL	Interleukin	**Rb**	Retinoblastoma protein

Sensitizing and T790M mutant EGFR tyrosine kinase inhibition

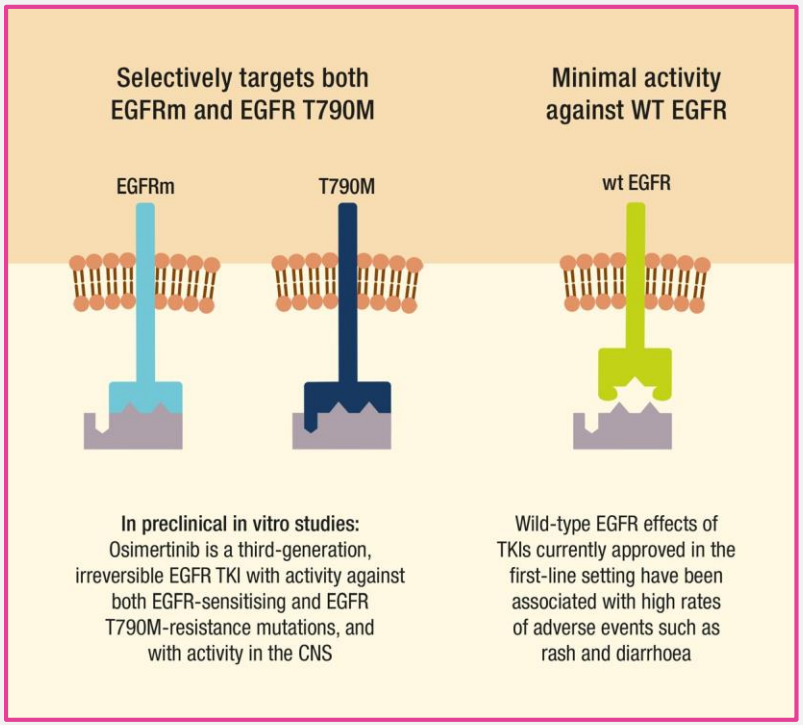
Osimertinib

Tumor Types: EGFRm NSCLC

Target Overview

Targeted inhibition of tumors harboring activating mutations in EGFR has helped to advance the treatment approach for advanced NSCLC.

While the majority of these activating mutations also sensitize EGFR (EGFRm) to effective targeting by early generation EGFR-TKIs, the emergence of a secondary resistance mutation (EGFR T790M) results in treatment-refractory NSCLC disease progression. Approximately 51%-68% of tumors that progress on a 1st and 2nd generation EGFR TKI are EGFR T790M mutation positive.[1-7]



Sensitizing and T790M mutant EGFR tyrosine kinase inhibition

Osimertinib

Tumor Types: EGFRm NSCLC

Compound Overview

Osimertinib is a third-generation, irreversible EGFR-TKI designed to selectively target both EGFR-sensitizing and EGFR T790M-resistance mutations.[1]

Osimertinib is being clinically evaluated in EGFRm-containing NSCLC.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

AstraZeneca

Sensitizing and T790M mutant EGFR tyrosine kinase inhibition

Osimertinib

Tumor Types: EGFRm NSCLC

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
1L EGFRm NSCLC (FLAURA2)	Osimertinib ± pemetrexed chemotherapy	III	NCT04035486
EGFRm + resectable NSCLC (NeoADAURA)	Osimertinib ± chemotherapy	III	NCT04351555
EGFRm Stage IB-IIIA NSCLC following complete tumor resection with or without adjuvant chemotherapy (ADAURA)	Osimertinib	III	NCT02511106
Stage III unresectable EGFRm NSCLC (LAURA)	Osimertinib	III	NCT03521154
Advanced EGFRm NSCLC with progression on an EGFR-TKI (TATTON)	Osimertinib in combination with savolitinib,[a] durvalumab, selumetinib	I	NCT02143466
EGFRm + locally advanced or metastatic NSCLC (ELIOS)[b]	Osimertinib	II	NCT03239340
Locally advanced or metastatic EGFRm/MET+ NSCLC following prior osimertinib therapy (SAVANNAH)	Osimertinib + savolitinib[a]	II	NCT03778229
Advanced NSCLC in patients who progressed on 1L osimertinib therapy (ORCHARD)	Osimertinib in combination with savolitinib[a] or gefitinib or necitumumab, or alectinib, or selpercatinib, or durvalumab in combination with carboplatin and pemetrexed	II	NCT03944772
EGFRm NSCLC and brain metastases (ODIN-BM)	Radiolabeled [11C] osimertinib	I	NCT03463525
Advanced EGFRm NSCLC with LM metastasis or brain metastasis following progression on an EGFR-TKI and chemotherapy (BLOOM)	Osimertinib (LM only), AZD3759	I	NCT02228369

[a]Savolitinib, partnered with Hutchison MediPharma Limited; [b]Post osimertinib translational biomarker study.

Sensitizing and T790M mutant EGFR tyrosine kinase inhibition

Tumor Types: EGFRm NSCLC

References

1. Cross DA, Ashton SE, Ghiorghiu SE, et al. *Cancer Discov*. 2014;4(9):1046-1061.
2. Yu HA, Arcila ME, Rekhtman N, et al. *Clin Cancer Res*. 2013;19(8):2240-2247.
3. Oxnard GR, Arcila ME, Sima CS, et al. *Clin Cancer Res*. 2011;17(6):1616-1622.
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5. Arcila ME, Oxnard GR, Nafa K, et al. *Clin Cancer Res*. 2011;17(5):1169-1180.
6. Kuiper JL, Heideman DA, Thunnissen E, et al. *Lung Cancer*. 2014;85(1):19-24.
7. Li W, Ren S, Li J, et al. *Lung Cancer*. 2014;84(3):295-300.

Osimertinib

Sensitizing and T790M mutant EGFR tyrosine kinase inhibition

Tumor Types: EGFRm NSCLC

Abbreviations

View all abbreviations & acronyms

1L	First line	**NSCLC**	Non-small-cell lung cancer
CNS	Central nervous system	**LM**	Leptomeningeal
EGFR	Epidermal growth factor receptor	**TKI**	Tyrosine kinase inhibitor
EGFRm	Epidermal growth factor receptor mutation	**WT**	Wild type

VEGFR tyrosine kinase inhibition

Cediranib

Tumor Types: Platinum-resistant and -sensitive ovarian cancer, and Advanced solid tumors

Target Overview

Inhibition of VEGFR tyrosine kinase activity interferes with tumor angiogenesis/vascularization and might result in tumor cell death.[1]

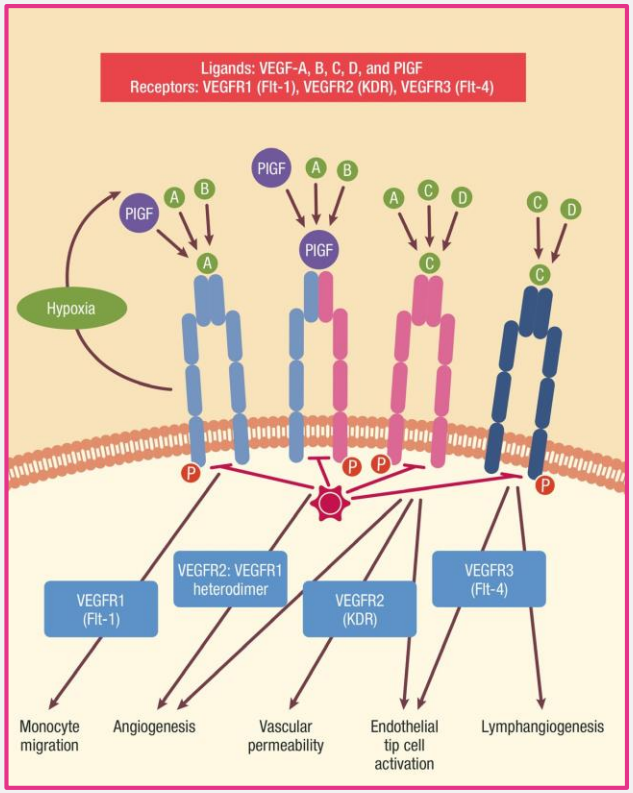


Figure adapted from Smith NR, Wedge SR, Pommier A, et al. *Biochem Soc Trans*. 2014;42(6):1601-1607.

VEGFR tyrosine kinase inhibition

Cediranib

Tumor Types: Platinum-resistant and -sensitive ovarian cancer, and Advanced solid tumors

Compound Overview

Cediranib is an orally bioavailable, selective inhibitor of the VEGFR tyrosine kinases VEGFR-1, VEGFR-2, and VEGFR-3,[2] which are overexpressed on many tumor cells.

Cediranib is being investigated as a maintenance treatment in patients with platinum-resistant and -sensitive, recurrent ovarian cancer.[3,4]

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

VEGFR tyrosine kinase inhibition

Cediranib

Tumor Types: Platinum-resistant and -sensitive ovarian cancer, and Advanced solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced solid tumors, recurrent ovarian cancer	Durvalumab + cediranib or olaparib	I/II	NCT02484404[a]
Advanced solid tumors	Cediranib + olaparib	II	NCT02498613[a]
Platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer (COCOS)	Cediranib or cediranib + olaparib	II/III	NCT02502266[a]
Platinum-resistant ovarian cancer (CONCERTO)	Cediranib + olaparib	IIb	NCT02889900

[a]This study is sponsored by the US National Cancer Institute (NCI).

VEGFR tyrosine kinase inhibition

Cediranib

Tumor Types: Platinum-resistant and -sensitive ovarian cancer, and Advanced solid tumors

References

1. Moreira IS, Fernandes PA, Ramos MJ. *Anticancer Agents Med Chem*. 2007;7(2):223-245.
2. Wedge SR, Kendrew J, Hennequin LF, et al. *Cancer Res*. 2005;65(10):4389-4400.
3. Liu JF, Barry WT, Birrer M, et al. *Lancet Oncol*. 2014;15(11):1207-1214.
4. Scambia G, Salutari V, Ferrandina G. *Lancet Oncol*. 2014;15(11):1179-1181.

VEGFR tyrosine kinase inhibition

Cediranib

Tumor Types: Platinum-resistant and -sensitive ovarian cancer, and Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

Flt1	Fms-related tyrosine kinase 1	**VEGF**	Vascular endothelial growth factor
Flt4	Fms-related tyrosine kinase 4	**A**	VEGF ligand A
KDR	Kinase insert domain receptor	**B**	VEGF ligand B
PlGF	Placental growth factor	**C**	VEGF ligand C
VEGFR	Vascular endothelial growth factor receptor	**D**	VEGF ligand D

MEK inhibition

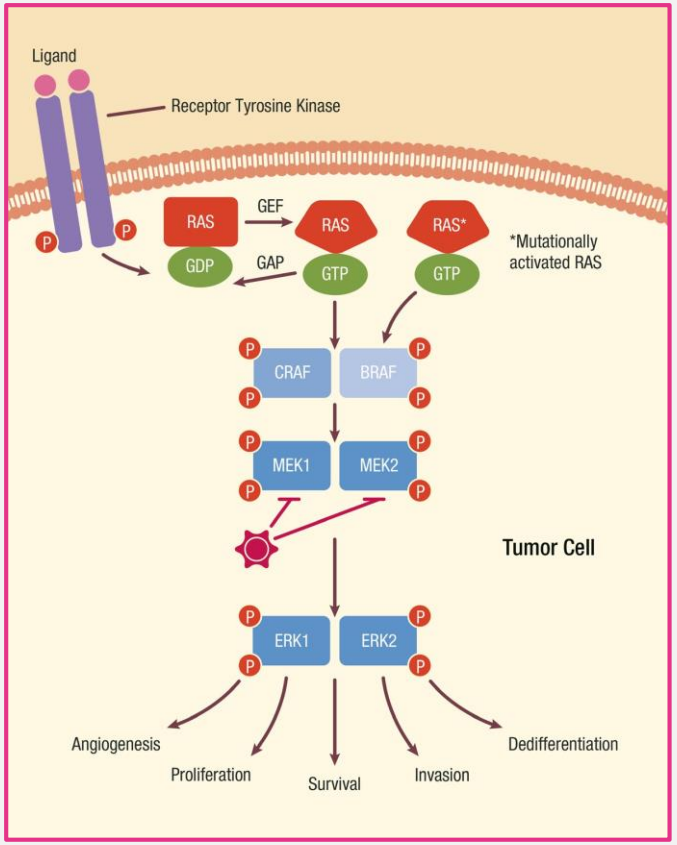
Selumetinib

Tumor Types: Neurofibromatosis type 1 (NF1)

Target Overview

The MAPK/ERK pathway (also known as the Ras-Raf-MEK-ERK pathway) is a cell-signaling pathway that plays a vital role in normal cell division and growth. Mutations that result in constitutive activation of the MAPK/ERK pathway have been implicated in a broad range of solid tumors and are associated with tumors resistant to standard cancer therapies.[1-3]

Inhibition of MEK1 and MEK2, 2 pivotal protein kinases in the MAPK/ERK pathway, may block solid tumor growth and interfere with development of resistance.[4,5]



MEK inhibition

Selumetinib

Tumor Types: Neurofibromatosis type 1 (NF1)

Compound Overview

Selumetinib[a] is an oral, highly selective allosteric MEK1/2 inhibitor with a short half-life that is being investigated in a variety of MEK-dependent tumors.

[a]Selumetinib is licensed from Array BioPharma Inc.

Some compounds illustrated from AstraZeneca may refer to selected pipeline products still under investigation and development. AstraZeneca pipeline products are investigational products and, as such, are not approved by the US Food & Drug Administration (FDA), the European Medicines Agency (EMA), or any other regulatory agency for the uses under investigation. Information regarding these investigational products should under no circumstances be regarded as a recommendation for their use or of their safety or efficacy.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

MEK inhibition

Selumetinib

Tumor Types: Neurofibromatosis type 1 (NF1)

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Pediatric NF1-associated inoperable plexiform neurofibromas	Selumetinib	I/II	NCT01362803[a]

[a]This study is sponsored by the US National Cancer Institute (NCI).

MEK inhibition

Selumetinib

Tumor Types: Neurofibromatosis type 1 (NF1)

References

1. Platz A, Egyhazi S, Ringborg U, et al. *Mol Oncol*. 2008;1(4):395-405.
2. Shields DJ, Murphy EA, Desgrosellier JS, et al. *Oncogene*. 2011;30(18):2123-2134.
3. Lee JH, Choi JW, Kim YS. *Br J Dermatol*. 2011;164(4):776-784.
4. Davies BR, Logie A, McKay JS, et al. *Mol Cancer Ther*. 2007;6(8):2209-2219.
5. Eberhard DA, Johnson BE, Amler LC, et al. *J Clin Oncol*. 2005;23(25):5900-5909.

MEK inhibition

Selumetinib

Tumor Types: Neurofibromatosis type 1 (NF1)

Abbreviations

View all abbreviations & acronyms

ERK	Extracellular signal-regulated kinase	**MEK**	Mitogen/extracellular signal-regulated kinase
GAP	Guanosine triphosphatase-activating protein	**RAF**	Rapidly accelerated fibrosarcoma
GEF	Guanine nucleotide exchange factor	**RAS**	Rat sarcoma
GDP	Guanosine diphosphate	**GTP**	Guanosine triphosphate
MAPK	Mitogen-activated protein kinase		

AKT inhibition

Capivasertib

Tumor Types: Breast cancer, Gynecologic cancers, Metastatic castration-resistant prostate cancer

Target Overview

The cell signaling network, which includes PI3K, AKT (protein kinase B), and mTOR, is frequently deregulated in human cancer. AKT is a central node in this network, modulating a range of substrates involved in growth, apoptosis, and metabolism. There are 3 isoforms of AKT: AKT1, 2, and 3. The most commonly mutated genes that result in activation of AKT proteins are activating mutations in AKT1 and PIK3CA and inactivating mutations in PTEN.[1,2]

AKT activation has been shown to mediate resistance to inhibitors of receptor tyrosine kinases, antihormonal agents, and chemotherapy.[3]

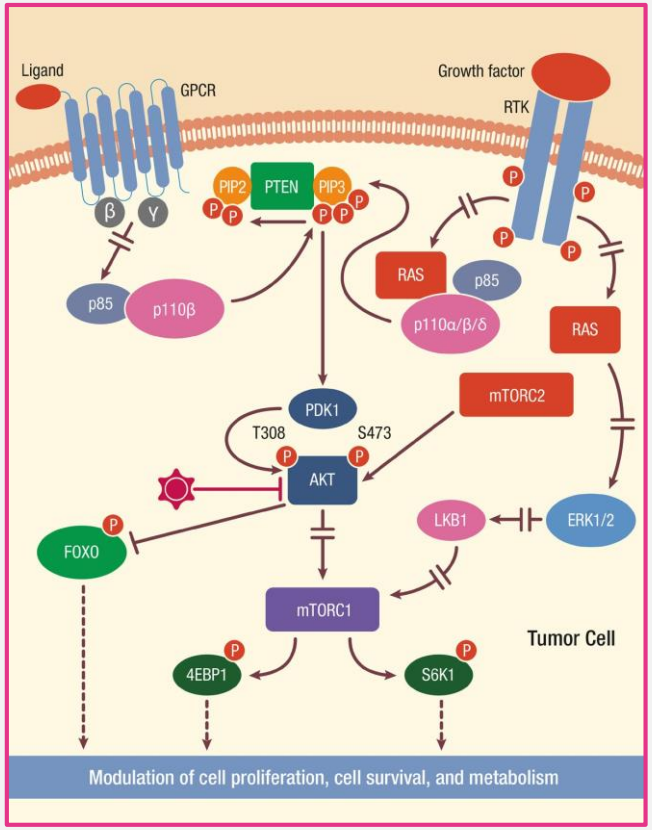


Figure adapted from Martini M, De Santis MC, Braccini L, et al. *Ann Med*. 2014;46(6):372-383.

AKT inhibition

Capivasertib

Tumor Types: Breast cancer, Gynecologic cancers, Metastatic castration-resistant prostate cancer

Compound Overview

Capivasertib,[a] an investigational pan-AKT kinase inhibitor (against isoforms AKT1, AKT2, and AKT3), is being clinically evaluated as a potential treatment for advanced solid tumor.[4]

[a]Formerly known as AZD5363, discovered by AstraZeneca subsequent to a collaboration with Astex Therapeutics (and its collaboration with the Institute of Cancer Research and Cancer Research Technology Limited).

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

AKT inhibition

Capivasertib

Tumor Types: Breast cancer, Gynecologic cancers, Metastatic castration-resistant prostate cancer

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced or metastatic breast, gynecologic cancers or other solid cancers bearing either AKT1 or PTEN mutation	Capivasertib	I	NCT01226316
Metastatic castration-resistant prostate cancer (ProCAID)	Docetaxel + prednisolone ± capivasertib	I/II	NCT02121639[a]
Metastatic TNBC (BEGONIA)	Capivasertib or danvatirsen or oleclumab or durvalumab + paclitaxel or trastuzumab deruxtecan	I/II	NCT03742102
Metastatic TNBC, IL (CAPItello-290)	Paclitaxel ± capivasertib	III	NCT03997123

[a]This study is sponsored by the University Hospital Southampton NHS Foundation Trust, United Kingdom;

AKT inhibition

Capivasertib

Tumor Types: Breast cancer, Gynecologic cancers, Metastatic castration-resistant prostate cancer

References

1. Altomare DA, Testa JR. *Oncogene*. 2005;24(50):7455-7464.
2. Liu P, Cheng H, Roberts TM, et al. *Nat Rev Drug Discov*. 2009;8(8):627-644.
3. Clark AS, West K, Streicher S, et al. *Mol Cancer Ther*. 2002;1(9):707-717.
4. Davies BR, Greenwood H, Dudley P, et al. *Mol Cancer Ther.* 2012;11(4):873-887.

AKT inhibition

Capivasertib

Tumor Types: Breast cancer, Gynecologic cancers, Metastatic castration-resistant prostate cancer

Abbreviations

View all abbreviations & acronyms

EIF4EBP1	Eukaryotic translation initiation factor 4E binding protein 1
AKT	Protein kinase B
ERK	Extracellular signal-regulated kinase
FOXO	Forkhead box protein O subclass
LKB1	Liver kinase B1
mTORC	Mammalian target of rapamycin complex
PI3KCA	Phosphatidylinositol 3-kinase
p85	Regulatory subunit of PI3K
p110	Catalytic subunit of PI3K
PDK	Phosphoinositide-dependent kinase
PI3K	Phosphoinositide 3-kinase
PIP2	Phosphatidylinositol 3,4-bisphosphate
PIP3	Phosphatidylinositol 3,4,5-bisphosphate
PTEN	Phosphatase and tensin homolog
RAS	Rat sarcoma
RTK	Receptor tyrosine kinase
S6K	Ribosomal subunit 6 kinase
TNBC	Triple negative breast cancer
GPCR	G protein coupled receptor

MET inhibition

Savolitinib

Tumor Types: MET-driven NSCLC

Target Overview

Aberrant activation of the MET receptor tyrosine kinase pathway through mutation, gene amplification, or protein overexpression has been implicated in oncogenesis and tumor cell growth.[1,2]

Alterations in the MET signaling are associated with papillary renal cell carcinoma and gastric, lung, and colorectal cancers.[3-6]

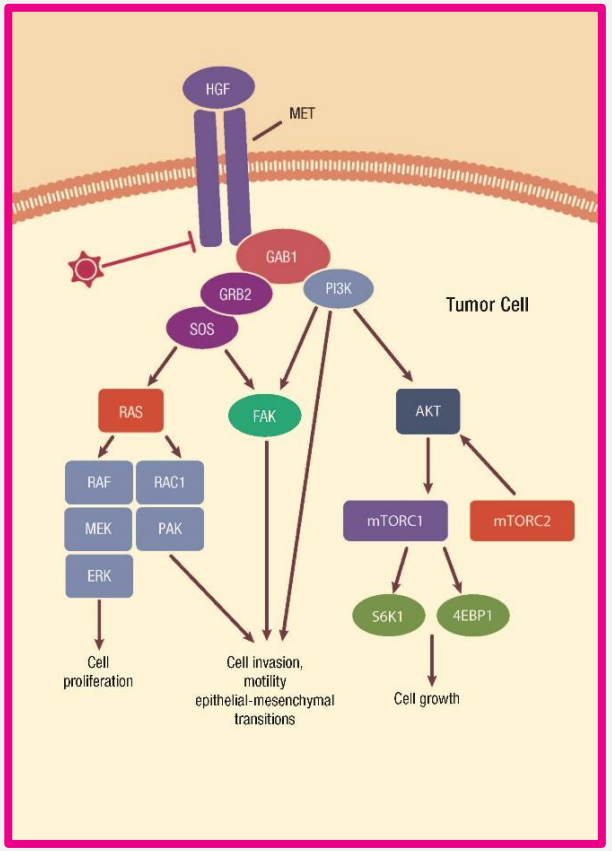


Figure adapted from Eder JP, Vande Woude GF, Boerner SA, et al. *Clin Cancer Res*. 2009;15(7):2207-2214.

MET inhibition

Savolitinib

Tumor Types: MET-driven NSCLC

Compound Overview

Savolitinib[a] is an investigational, selective MET inhibitor that is being clinically evaluated as a potential treatment for NSCLC cancer and other cancers.

[a]Savolitinib, partnered with Hutchison MediPharma Limited.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

MET inhibition

Savolitinib

Tumor Types: MET-driven NSCLC

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced EGFRm NSCLC with progression on an EGFR-TKI (TATTON)	Osimertinib + savolitinib[a] or durvalumab, or selumetinib	I	NCT02143466
Exon14 skipping alteration lung sarcomatoid carcinoma / NSCLC	Savolitinib[a]	II	NCT02897479
Locally advanced or metastatic EGFRm/MET+ amplification NSCLC following prior osimertinib therapy (SAVANNAH)	Osimertinib + savolitinib[a]	II	NCT03778229
Advanced NSCLC in patients who progressed on 1L osimertinib therapy (ORCHARD)	Osimertinib + savolitinib[a] or gefitinib or necitumumab or alectinib or selpercatinib Durvalumab + carboplatin + pemetrexed	II	NCT03944772

[a]Savolitinib, partnered with Hutchison MediPharma Limited.

MET inhibition

Savolitinib

Tumor Types: MET-driven NSCLC

References

1. Organ SL, Tsao MS. *Ther Adv Med Oncol*. 2011;31(1 suppl):S7-S19.
2. Maroun CR, Rowlands T. *Pharmacol Ther*. 2014;142(3):316-338.
3. Olivero M, Valente G, Bardelli A, et al. *Int J Cancer*. 1999;82(5):640-643.
4. Schmidt L, Junker K, Nakaigawa N, et al. *Oncogene*. 1999;18(14):2343-2350.
5. Sierra JR, Tsao MS. *Ther Adv Med Oncol*. 2011;3(1 suppl):S21-S35.
6. Bardelli A, Corso S, Bertotti A, et al. *Cancer Discov*. 2013;3(6):658-673.

MET inhibition

Savolitinib

Tumor Types: MET-driven NSCLC

Abbreviations

View all abbreviations & acronyms

1L	First line	**EGFR**	Epidermal growth factor receptor	**EGFRm**	Epidermal growth factor receptor mutation
mTORC	Mammalian target of rapamycin complex	**TKI**	Tyrosine kinase inhibitor	**RAC**	Ras-related C3 botulinum toxin substrate
EIF4EBP1	Eukaryotic translation initiation factor 4E binding protein 1	**GAB2**	GRB2-associated binding protein 2	**RAF**	Rapidly accelerated fibrosarcoma
AKT	Protein kinase B	**HGF**	Hepatocyte growth factor	**RAS**	Rat sarcoma
ERK	Extracellular signal-regulated kinase	**MEK**	Mitogen/extracellular signal-regulated kinase	**S6K**	Ribosomal subunit 6 kinase
FAK	Focal adhesion kinase	**NSCLC**	Non-small-cell lung cancer	**SOS**	Son of sevenless
GAB1	GRB2-associated binding protein 1	**PAK**	p21 activated kinase	**PI3K**	Phosphoinositide 3-kinase

PI3K β/δ inhibition

AZD8186

Tumor Types: Advanced solid tumors

Target Overview

The PI3K/AKT/mTOR signaling network is a critical regulator of many cellular processes, including normal cell proliferation, survival, and growth. Increased cellular activity of PI3 kinases, either through functional loss of the PTEN tumor suppressor protein (PI3 kinase antagonist) or PI3 kinase activation mutations, is associated with development of many tumor types and hematologic malignancies.[1-3]

Two PI3 kinase isoforms, PI3Kβ and PI3Kδ, have been clinically validated as targets in a variety of cancers and malignancies.[1,2]

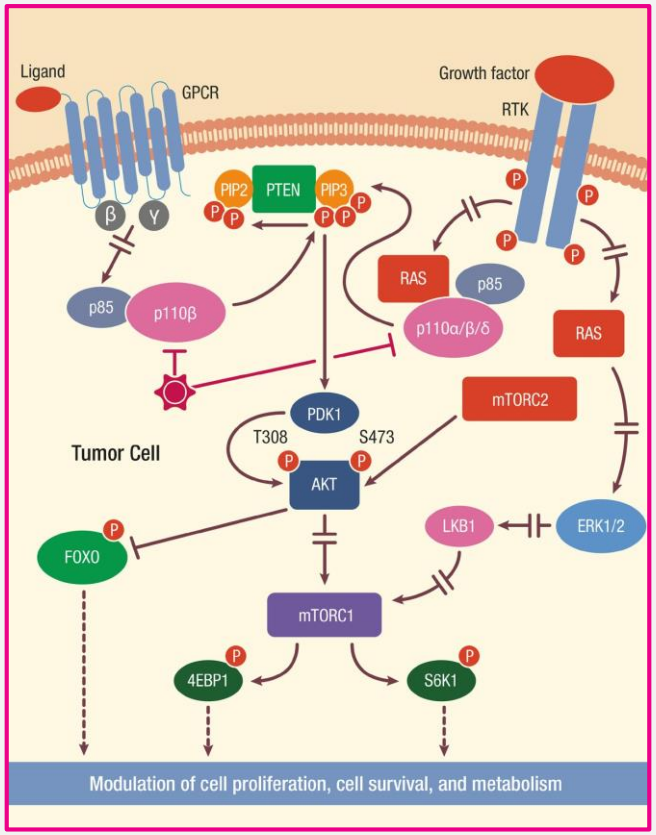


Figure adapted from Martini M, De Santis MC, Braccini L, et al. *Ann Med*. 2014;46(6):372-383.

PI3K β/δ inhibition

AZD8186

Tumor Types: Advanced solid tumors

Compound Overview

AZD8186, a potent inhibitor of PI3Kβ/δ with activity against PI3Kβ/δ signaling, has the potential to reduce the growth of tumors dependent on dysregulated PTEN. AZD8186 is being investigated for use in advanced solid tumors.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

PI3K β/δ inhibition

AZD8186

Tumor Types: Advanced solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
PTEN mutated or PIK3CB mutated advanced solid tumors	AZD8186 + docetaxel	I	NCT03218826[a]

[a]This study is sponsored by the US National Cancer Institute (NCI).

PI3K β/δ inhibition

AZD8186

Tumor Types: Advanced solid tumors

References

1. Hancox U, Cosulich S, Hanson L, et al. *Mol Cancer Ther*. 2015;14(1):48-58.
2. Barlaam B, Cosulich S, Degorce S, et al. *J Med Chem*. 2015;58(2):943-962.
3. Schwartz S, Wongvipat J, Trigwell CB, et al. *Cancer Cell*. 2015;27(1):109-122.

PI3K β/δ inhibition

AZD8186

Tumor Types: Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

EIF4EBP1	Eukaryotic translation initiation factor 4E binding protein 1	**mTORC**	Mammalian target of rapamycin complex	**mTOR**	Mammalian target of rapamycin
AKT	Protein kinase B	**p85**	Regulatory subunit of PI3K	**PTEN**	Phosphatase and tensin homolog
CRPC	Castration-resistant prostate cancer	**p110**	Catalytic subunit of PI3K	**RAS**	Rat sarcoma
ERK	Extracellular signal-regulated kinase	**PDK**	Phosphoinositide-dependent kinase	**RTK**	Receptor tyrosine kinase
FOXO	Forkhead box protein O subclass	**PI3K**	Phosphoinositide 3-kinase	**S6K**	Ribosomal subunit 6 kinase
GPCPR	G protein-coupled receptor	**PIP2**	Phosphatidylinositol 3,4-bisphosphate	**sqNSCLC**	Squamous non-small-cell lung cancer
LKB1	Liver kinase B1	**PIP3**	Phosphatidylinositol 3,4,5-bisphosphate	**TNBC**	Triple negative breast cancer
PI3	Peptidase Inhibitor 3	**PIK3CB**	Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Beta		

ERα degradation and antagonism

AZD9833

Tumor Types: ER+, HER2- breast cancer

Target Overview

Estrogen receptor alpha (ERα) is expressed in about 70% of breast cancer cases.[1] ERα activity is essential for ER+ breast cancers, and while they may respond well to anti-estrogen therapies such as aromatase inhibitors (AIs) and selective estrogen receptor modulators (SERMs),[2] resistance can emerge.[3]

SERDs antagonize ERα and target it for degradation.[4]

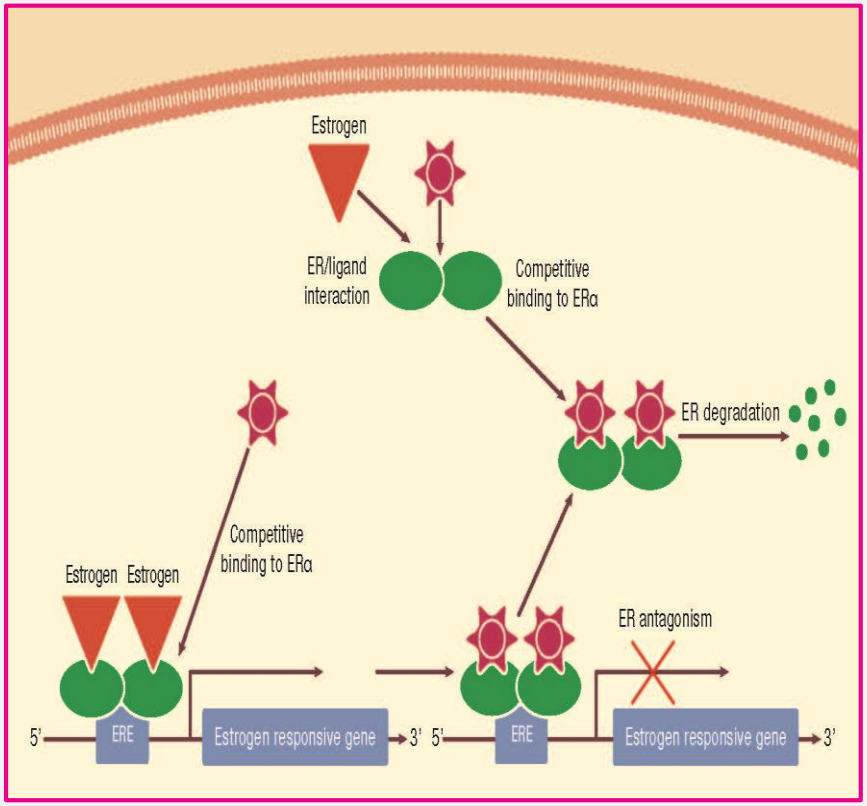


Figure adapted from Ratanaphan A. *Int J Mol Sci*. 2012;13(11):14898-14916.

ERα degradation and antagonism

AZD9833

Tumor Types: ER+, HER2- breast cancer

Compound Overview

AZD9833 is an investigational oral, nonsteroidal ERα antagonist and selective estrogen receptor degrader. The molecule is being clinically evaluated as a potential treatment for ER+, HER2- breast cancers.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

ERα degradation and antagonism

AZD9833

Tumor Types: ER+, HER2- breast cancer

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
ER+, HER2- advanced breast cancer (SERENA-1)	AZD9833 ± palbociclib	I	NCT03616587
ER+, HER2- advanced breast cancer (SERENA-2)	AZD9833, fulvestrant	II	NCT04214288

ERα degradation and antagonism

AZD9833

Tumor Types: ER+, HER2- breast cancer

References

1. Li CI, Daling JR, Malone KE. *J Clin Oncol*. 2003;21(1):28-34.
2. Early Breast Cancer Trialists' Collaborative Group. *Lancet.* 2005;365(9472):1687-1717.
3. Jeselsohn R, Buchwalter G, De Angelis C, et al. *Nat Rev Clin Oncol.* 2015;12(10):573-583.
4. Gombos A. *Curr Opin Oncol.* 2019;31(5):424-429.

ERα degradation and antagonism

AZD9833

Tumor Types: ER+, HER2- breast cancer

Abbreviations

View all abbreviations & acronyms

AI	Aromatase inhibitor
ER	Estrogen receptor
ERE	Estrogen response element
SERD	Selective estrogen receptor degrader
SERM	Selective estrogen receptor modulator
HER2	Human epidermal growth factor receptor 2

BTK inhibition

Acalabrutinib

Tumor Types: Hematologic malignancies

Target Overview

Bruton tyrosine kinase (BTK) plays a critical role in the B cell antigen receptor signaling pathway, which is responsible for normal B-cell development, function, and survival.[1,2]

BTK has been implicated in the pathogenesis of B-cell malignancies and has recently emerged as an important therapeutic target.[1,2]

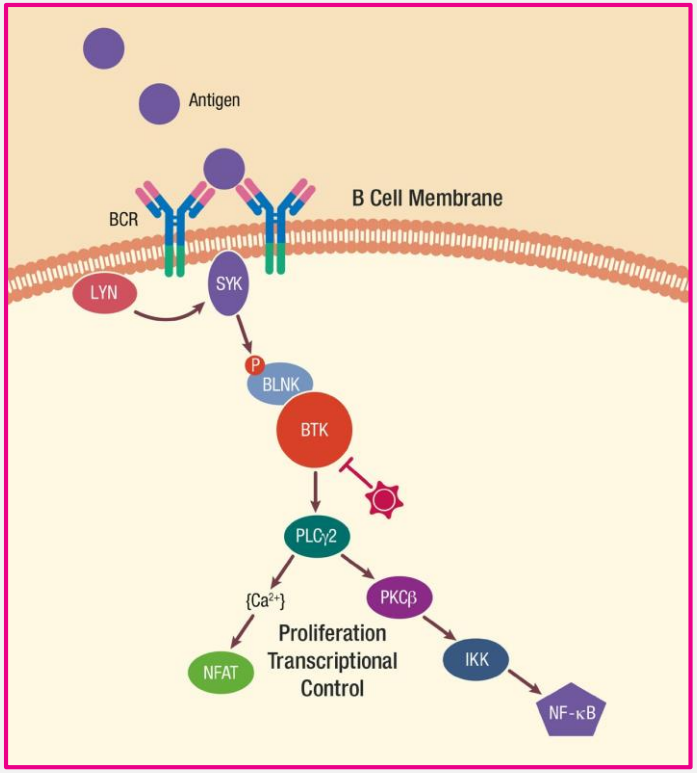


Figure adapted from references (3) and (4)

BTK inhibition

Acalabrutinib

Tumor Types: Hematologic malignancies

Compound Overview

Acalabrutinib[a] is a potent, highly selective inhibitor of BTK.[3] Acalabrutinib is currently being evaluated in multiple Phase I, II, and III clinical trials.

[a]Acalabrutinib is being developed in collaboration with Acerta Pharmaceuticals.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

BTK inhibition

Acalabrutinib

Tumor Types: Hematologic malignancies

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Previously untreated MCL	Acalabrutinib, bendamustine, rituximab vs. placebo, bendamustine, rituximab	III	NCT02972840
Previously untreated CLL	Acalabrutinib vs. acalabrutinib + obinutuzumab vs. obinutuzumab + chlorambucil	III	NCT02475681
Previously treated high-risk CLL	Acalabrutinib vs. ibrutinib	III	NCT02477696
Relapsed/refractory CLL	Acalabrutinib vs. bendamustine-rituximab or idelalisib-rituximab	III	NCT02970318
Relapsed/refractory CLL and intolerant to ibrutinib	Acalabrutinib	II	NCT02717611
Relapsed/refractory CLL	Ceralasertib Ceralasertib ± acalabrutinib	I/II	NCT03328273
Relapsed/refractory aggressive non-Hodgkin's Lymphoma (PRISM Study)	AZD5153 + acalabrutinib AZD9150 + acalabrutinib Ceralasertib + acalabrutinib Hu5F9-G4 + rituximab + acalabrutinib	I	NCT03527147

BTK inhibition

Acalabrutinib

Tumor Types: Hematologic malignancies

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Relapsed/refractory MCL or CLL, or B-cell malignancies	Acalabrutinib	I/II	NCT03932331
B-cell non-Hodgkin lymphoma, R/R FL	Acalabrutinib alone or in combination with rituximab ± lenalidomide	I/II	NCT02180711
Previously untreated CLL	Acalabrutinib + venetoclax vs. acalabrutinib + venetoclax ± obinutuzumab vs. chemoimmunotherapy	III	NCT03836261
Previously untreated CLL	Acalabrutinib vs. chlorambucil + rituximab	III	NCT04075292
Untreated and R/R CLL (ASSURE)	Acalabrutinib	III	NCT04008706
COVID-19 (CALAVI – US)	Acalabrutinib	II	NCT04380688[a]
COVID-19 (CALAVI – Global)	Acalabrutinib	II	NCT04346199[a]

[a]This is a non-oncology study

BTK inhibition

Acalabrutinib

Tumor Types: Hematologic malignancies

References

1. Horwood NJ, Urbaniak AM, Danks L. *Int Rev Immunol*. 2012;31(2):87-103.
2. Akinleye A, Chen Y, Mukhi N, et al. *J Hematol Oncol*. 2013;6:59.
3. Woyach JA, Johnson AJ, Byrd JC. *Blood*. 2012;120(6):1175-1184.
4. Ten Hacken E, Burger JA. *Clin Cancer Res*. 2014;20(3):548-556.
5. Byrd JC, Harrington B, O'Brien S, et al. *N Engl J Med*. 2016;374:323-332.

BTK inhibition

Acalabrutinib

Tumor Types: Hematologic malignancies

Abbreviations

View all abbreviations & acronyms

BCR	B-cell receptor
BLNK	B-cell linker
BTK	Bruton tyrosine kinase
CLL	Chronic lymphocytic leukemia
IKK	I kappa B kinase
LYN	Lck/Yes-related novel tyrosine kinase
PLC	Phospholipase C
MCL	Mantle cell lymphoma
NF-kB	Nuclear factor kappa-light-chain-enhancer of activated B-cells
R/R FL	Relapsed/refractory follicular lymphoma
NFAT	Nuclear factor of activated T cells
PKC	Protein kinase C
SYK	Spleen tyrosine kinase

MCL1 inhibition

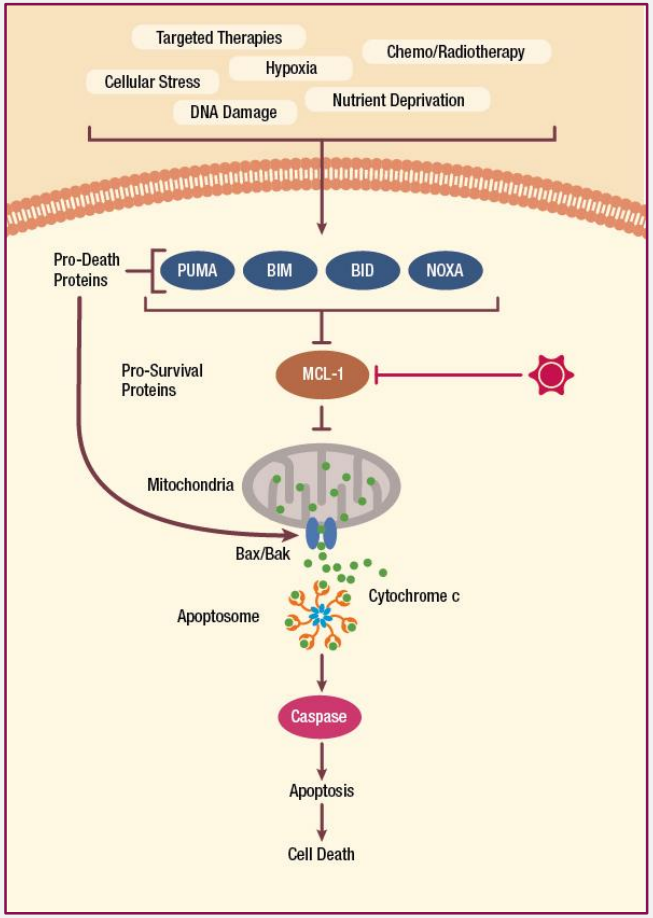
AZD5991

Tumor Types: Hematologic malignancies

Target Overview

MCL1 is a pro-survival member of the BCL2 family of proteins and is frequently overexpressed in human cancers. MCL1 inhibits apoptotic cell death, leading to the survival and proliferation of cancer cells.

BH3 mimetics are a class of compounds designed to disrupt the protein-protein interactions between pro-survival BCL2 family members (including BCL2, BCL-XL, and MCL1) and pro-apoptotic BCL2 family members (including BIM, NOXA, BAK, and BAX) and induce cancer cell death.[1-3]



MCL1 inhibition

AZD5991

Tumor Types: Hematologic malignancies

Compound Overview

AZD5991 is a potent and selective BH3 mimetic specifically designed to disrupt MCL1 protein complexes, while sparing BCL2 and BCL-XL protein complexes.[4]

AZD5991 is currently being investigated as a potential monotherapy and combination therapy in hematologic malignancies.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

MCL1 inhibition

AZD5991

Tumor Types: Hematologic malignancies

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Relapsed/refractory hematologic malignancies	AZD5991± venetoclax	I	NCT03218683

MCL1 inhibition

AZD5991

Tumor Types: Hematologic malignancies

References

1. Tron AE, Belmonte MA, Adam A, et al. *Nat Comm*. 2018;9(1):5341.
2. Czabotar PE, Lessene G, Strasser A, et al. *Nat Rev Mol Cell Biol*. 2014;15(1):49-63.
3. Delbridge AR, Strasser A. *Cell Death Differ*. 2015;22(7):1071-1080.
4. Belmonte MA, Adam A, Borrelli D, et al. *Blood.* 2014;124:3428.

MCL1 inhibition

AZD5991

Tumor Types: Hematologic malignancies

Abbreviations

View all abbreviations & acronyms

BAK	BCL2-homologous antagonist/killer
BAX	BCL2-associated X protein
BCL2	B-cell lymphoma 2
BCL-XL	B-cell lymphoma extra large
BH3	BCL2 homology domain 3
NOXA	Phorbol-12-myristate-13-acetate-induced protein 1
BIM	BCL2-interacting mediator of cell death
FADD	Fas-associated death domain
MCL1	Myeloid cell leukemia 1
PUMA	p53-upregulated modulator of apoptosis
BID	BH3-interacting-domain death agonist

AstraZeneca

CDK9 inhibition

AZD4573

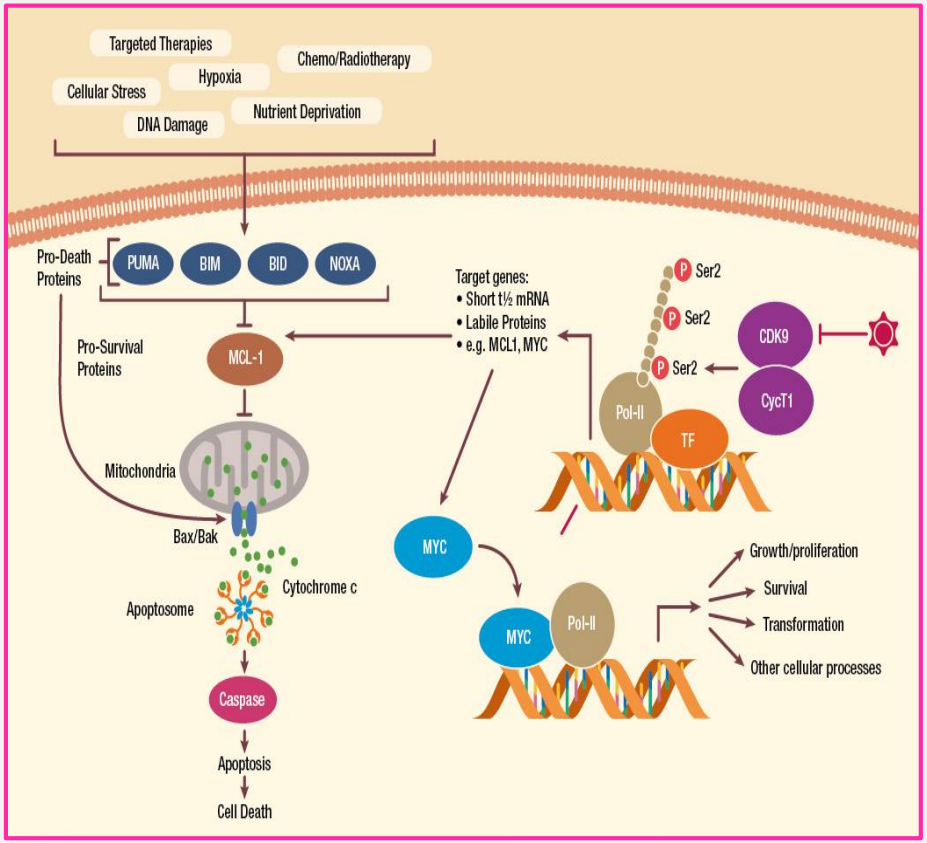
Tumor Types: Hematologic malignancies

Target Overview

CDK9 is a serine/threonine kinase that regulates elongation of transcription through phosphorylation of RNA polymerase II at serine 2.[1]

Short-term inhibition of CDK9 results in transient transcriptional repression and rapid downregulation of genes with short-lived mRNAs and labile proteins, including MCL1 and MYC.[2]

CDK9 inhibition, therefore, represents an attractive approach to indirectly target these oncoproteins as a monotherapy and in combination with other agents.



CDK9 inhibition

AZD4573

Tumor Types: Hematologic malignancies

Compound Overview

AZD4573 is a highly potent and selective CDK9 inhibitor that decreases phosphorylation levels of RNA polymerase II and rapidly reduces levels of MCL1 and MYC, leading to induction of apoptosis and antitumor activity in multiple tumor models.

AZD4573 is currently being evaluated in the clinic for safety and efficacy as a monotherapy in hematologic malignancies. Combination treatments are also under investigation for AZD4573.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

CDK9 inhibition

AZD4573

Tumor Types: Hematologic malignancies

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Relapsed/refractory hematologic malignancies	AZD4573	I	NCT03263637

CDK9 inhibition

AZD4573

Tumor Types: Hematologic malignancies

References

1. Bowman EA, Kelly WG. *Nucleus*. 2014;5(3):224-236.
2. Booher RN, Hatch H, Dolinski BM, et al. *PLoS One*. 2014;9(10):e108371.

CDK9 inhibition

AZD4573

Tumor Types: Hematologic malignancies

Abbreviations

View all abbreviations & acronyms

BIM	BCL2-interacting mediator of cell death
BID	BH3-interacting domain death agonist
BAX	BCL2-associated X protein
CDK9	Cyclin-dependent kinase 9
CycT1	Cyclin T1
MCL1	Myeloid cell leukemia 1
MYC	Myelocytomatosis viral oncogene
PI3K	Phosphoinositide 3-kinase
BAK	BCL2-homologous antagonist/killer
NOXA	Phorbol-12-myristate-13-acetate-induced protein 1
Pol-II	RNA polymerase II
PUMA	p53 upregulated modulator of apoptosis
TF	Tissue factor
mRNA	Messenger RNA

BRD4 inhibition

AZD5153

Tumor Types: Advanced solid tumors, Hematologic malignancies

Target Overview

BRD4 is a member of the BET family and contains 2 bromodomains that are responsible for binding acetylated lysine residues on histone tails and other nuclear proteins. BRD4 acts as a molecular bridge by coupling histone acetylation to oncogenic transcriptional activation contributing to cancer cell survival and proliferation.[1,2]

BRD4 regulates MYC and NF-kB target gene expression.[3,4] BRD4 inhibition can suppress homologous recombination, sensitizing tumors to PARP inhibition.[5] BRD4 inhibitors have also demonstrated synergy with replication stress-inducing agents, leading to antitumor efficacy.[6]

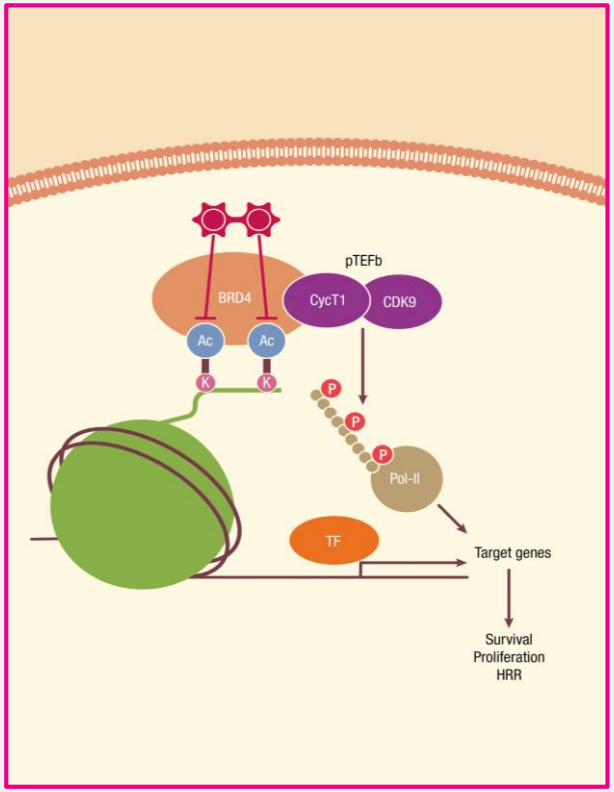


Figure adapted from Valent P, Zuber J. *Cell Cycle*. 2014;13(5):689-90.

BRD4 inhibition

AZD5153

Tumor Types: Advanced solid tumors, Hematologic malignancies

Compound Overview

AZD5153 is a potent, selective, oral, small-molecule inhibitor of BRD4/BET bromodomains capable of bivalent binding interaction ligating 2 bromodomains in BRD4.[7]

AZD5153 is currently being evaluated for safety and efficacy as a monotherapy and in combinations with advanced solid tumors, including lymphomas.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

BRD4 inhibition

AZD5153

Tumor Types: Advanced solid tumors, Hematologic malignancies

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Relapsed/refractory solid tumors, including lymphomas	AZD5153 ± olaparib	I	NCT03205176
Relapsed/refractory aggressive non-Hodgkin lymphoma (PRISM Study)	AZD5153 + acalabrutinib AZD9150 + acalabrutinib Ceralasertib + acalabrutinib Hu5F9-G4 + rituximab + acalabrutinib	I	NCT03527147

BRD4 inhibition

AZD5153

Tumor Types: Advanced solid tumors, Hematologic malignancies

References

1. Loven J, Hoke HA, Lin CY, et al. *Cell.* 2013;153(2):320-334.
2. Shi J, Vakoc CR. *Mol Cell.* 2014;54(5):728-736.
3. Mertz J, Conery A, Bryant B, et al. *Proc Natl Acad Sci.* 2011 Oct 4;108(40):16669-74.
4. Huang B, Yang X, Zhou M et al. *Mol Cell Biol.* 2009 Mar; 29(5):1375-1387.
5. Sun C, Yin J, Fang Y, et al. *Cancer Cell.* 2018 Mar 12;33(3):401-416.e8.
6. Zhang J, Dulak A, Hattersley M, et al. *Oncogene.* 2018 Jul;37(28):3763-3777.
7. Rhyasen GW, Hattersley MM, Yao Y, et al. *Mol Cancer Ther.* 2016;15(11):2563-2574.

BRD4 inhibition

AZD5153

Tumor Types: Advanced solid tumors, Hematologic malignancies

Abbreviations

View all abbreviations & acronyms

BET	Bromodomain and extra-terminal
BRD4	Bromodomain-containing protein 4
TF	Tissue factor
Pol II	RNA polymerase II
DDR	DNA damage response
PARP	Poly (ADP-ribose) polymerase
CDK9	Cyclin-dependent kinase 9

BCL2/BCL-XL inhibition

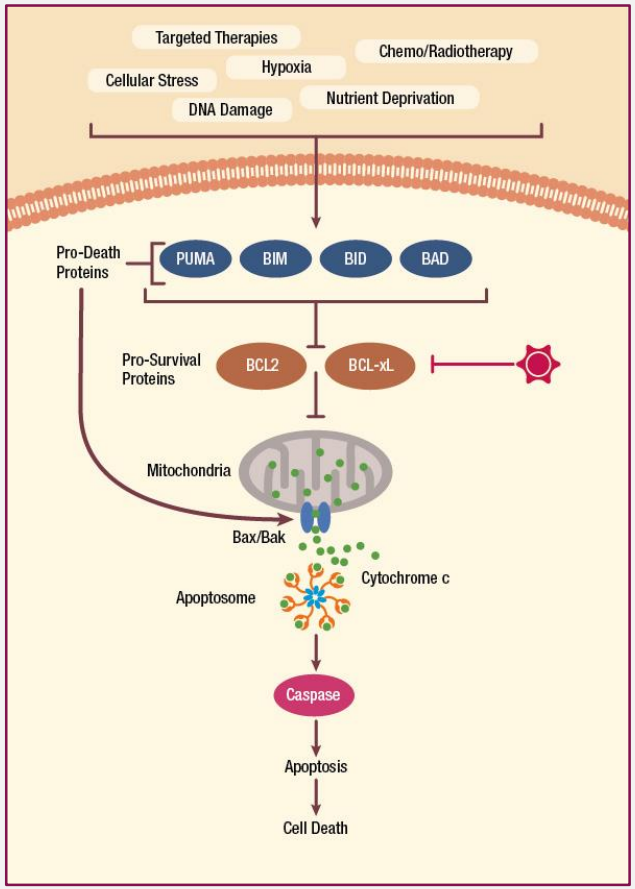
AZD0466

Tumor Types: Advanced hematologic or solid tumors

Target Overview

BCL2 and BCL-XL are 2 pro-survival proteins involved in the cell death or apoptosis pathway. They interact with pro-death BH3-only proteins, such as BIM and BID, and effectors BAX and BAK to promote cancer cell survival.[1]

High BCL2 expression is seen in patients with hematologic malignancies, while BCL-XL expression is correlated with decreased sensitivity to chemotherapy.[2] BH3 mimetics are a class of drugs that bind pro-survival proteins, disrupting their inhibition of pro-death proteins, resulting in cancer cell death.[3]



BCL2/BCL-XL inhibition

AZD0466

Tumor Types: Advanced hematologic or solid tumors

Compound Overview

AZD0466 is a nanomedicine of a potent inhibitor of BCL-2 and BCL-XL. AZD0466 conjugated with Starpharma DEP® biodegradable poly-L-lysine dendrimers[4] is specifically designed to disrupt both BCL-2 and BCL-XL interactions with pro-death proteins. AZD0466 administered on a weekly intravenous schedule releases the active moiety over a period of time to potentially maximize therapeutic index.

AZD0466 is currently being investigated as a potential therapy in both hematologic malignancies and solid cancers.

Tumor Drivers & Resistance Mechanisms

Pursuing innovative targeted approaches

Crafting molecules to inhibit oncogenic drivers with a high degree of specificity. Creating therapies and combinations that target intrinsic and acquired resistance, for a potentially more durable response.

BCL2/BCL-XL inhibition

AZD0466

Tumor Types: Advanced hematologic or solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced hematologic or solid tumors	AZD0466	I	NCT04214093

BCL2/BCL-XL inhibition

AZD0466

Tumor Types: Advanced hematologic or solid tumors

References

1. Czabotar PE, Lessene G, Strasser A, et al. *Nat Rev Mol Cell Biol*. 2014;15(1):49-63.
2. Delbridge AR, Strasser A. *Cell Death Differ*. 2015;22(7):1071-1080.
3. Merino D, Kelly GL, Lessene G, et al. *Cancer Cell.* 2018;34(6):879-891.
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BCL2/BCL-XL inhibition

AZD0466

Tumor Types: Advanced hematologic or solid tumors

Abbreviations

View all abbreviations & acronyms

BAK	BCL2-homologous antagonist/killer	**BIM**	BCL2-interacting mediator of cell death
BAX	BCL2-associated X protein	**DEP®**	Dendrimer drug delivery
BCL2	B-cell lymphoma 2	**BAD**	BCL-XL/BCL-2-associated death promoter
BCL-XL	B-cell lymphoma extra large	**PUMA**	p53-upregulated modulator of apoptosis
BH3	BCL2 homology domain 3	**BID**	BH3-interacting-domain death agonist

PARP inhibition

Olaparib

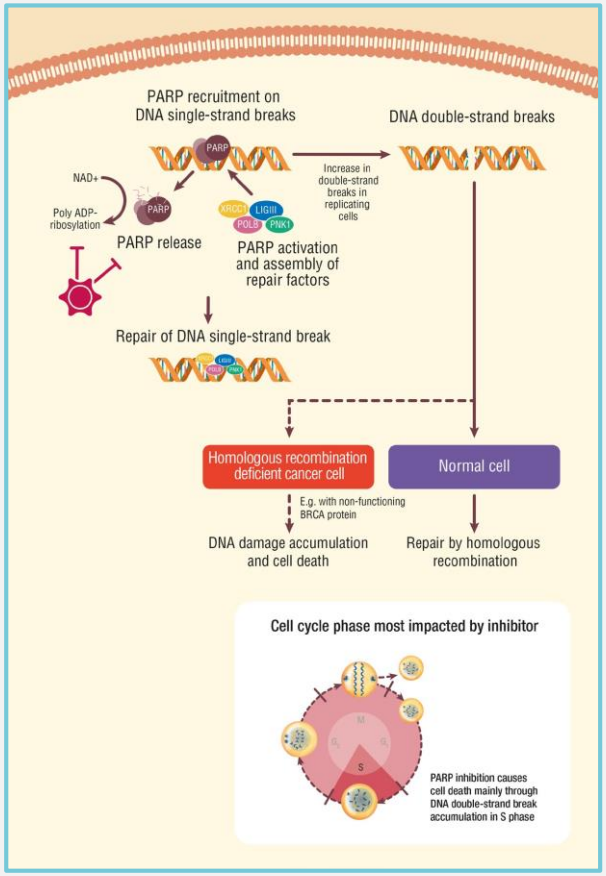
Tumor Types: Ovarian cancer, Breast cancer, Pancreatic cancer, Colorectal cancer, Prostate cancer, Endometrial cancer, Bladder cancer, Gastric cancer, NSCLC, and Advanced solid tumors

Target Overview

PARP (poly [ADP-ribose] polymerase) is a group of proteins, some of which are known to be involved in the repair of single-strand breaks in DNA.[1]

A healthy cell's DNA undergoes damage every day, with approximately 10,000 spontaneous single-strand breaks that require repair.[1]

Inhibition of PARP with olaparib leads to the trapping of PARP bound to DNA single-strand breaks, stalling of replication forks, their collapse and the generation of DNA double-strand breaks and cancer cell deaths. In tumor cells that already have compromised DNA repair mechanisms (such as loss of *BRCA1* or *BRCA2* function, affecting double-strand break repair), inhibition of PARP leads to excessive accumulation of DNA damage and may cause death of the cell.[1,2]



PARP inhibition

Olaparib

Tumor Types: Ovarian cancer, Breast cancer, Pancreatic cancer, Colorectal cancer, Prostate cancer, Endometrial cancer, Bladder cancer, Gastric cancer, NSCLC, and Advanced solid tumors

Compound Overview

Olaparib,[a] a PARP inhibitor, is being investigated in a range of DNA Damage Response Deficient tumors. Olaparib is being clinically evaluated in NSCLC, ovarian, bladder, breast, pancreatic, prostate, gastric, and other cancers.

[a]In collaboration with Merck & Co., Inc, Kenilworth, NJ, US (Merck: known as MSD outside of the US and Canada).

Some compounds illustrated from AstraZeneca may refer to selected pipeline products still under investigation and development. AstraZeneca pipeline products are investigational products and, as such, are not approved by the US Food & Drug Administration (FDA), the European Medicines Agency (EMA), or any other regulatory agency for the uses under investigation. Information regarding these investigational products should under no circumstances be regarded as a recommendation for their use or of their safety or efficacy.

DNA Damage Response

Exploiting pathway dependencies to potentially induce cancer death

PARP inhibition

Olaparib

Tumor Types: Ovarian cancer, Breast cancer, Pancreatic cancer, Colorectal cancer, Prostate cancer, Endometrial cancer, Bladder cancer, Gastric cancer, NSCLC, and Advanced solid tumors

Clinical Trial Information

Tumor	Setting	Regimen	Phase	Trial identifier
Ovarian cancer	Peritoneal or fallopian tube cancer (COCOS)	Olaparib, cediranib, olaparib + cediranib	II/III	NCT02502266[a]
	Peritoneal or fallopian tube cancer (LIGHT)	Olaparib	II	NCT02983799
	Recurrent platinum-sensitive ovarian, fallopian tube, or peritoneal cancer (GY004)	Olaparib ± cediranib	III	NCT02446600
	Peritoneal or fallopian tube cancer (L-MOCA)	Olaparib	III	NCT03534453
	Platinum-resistant (CONCERTO)	Olaparib + cediranib	II	NCT02889900
	BRCA+ and BRCA- (OReO)	Olaparib	III	NCT03106987
	BRCA or HRR+ mutated (ORZORA)	Olaparib	IV	NCT02476968
	Platinum-sensitive, relapsed, non-germline BRCAm (OPINION)	Olaparib	III	NCT03402841
	Advanced ovarian cancer (DUO-O)	Durvalumab + chemotherapy + bevacizumab followed by maintenance durvalumab, bevacizumab, and olaparib	III	NCT03737643
	Platinum Sensitive Relapsed Epithelial Ovarian Cancer (DUETTE)	Olaparib Ceralasertib + olaparib	II	NCT04239014

[a]This study is sponsored by the US National Cancer Institute (NCI).

PARP inhibition

Olaparib

Tumor Types: Ovarian cancer, Breast cancer, Pancreatic cancer, Colorectal cancer, Prostate cancer, Endometrial cancer, Bladder cancer, Gastric cancer, NSCLC, and Advanced solid tumors

Clinical Trial Information

Tumor	Setting	Regimen	Phase	Trial identifier
Breast cancer	Adjuvant (OlympiA)	Olaparib	III	NCT02032823
	Metastatic triple negative breast cancer stratified by BRCA1 or BRCA2 mutation (stratum A), mutation of other HRR pathway genes and no BRCA1 or BRCA2 mutation (stratum B), and no mutation of HRR genes (stratum C) (VIOLETTE)	Olaparib Olaparib + ceralasertib Olaparib + adavosertib	II	NCT03330847
	Metastatic breast cancer	Olaparib	III	NCT03286842
Pancreatic cancer	Metastatic	Olaparib	II	NCT02677038[a]
Colorectal Cancer	Metastatic	Olaparib ± bevacizumab	III	NCT04456699
NSCLC	Stage IV tumors that lack EGFR mutations and ALK fusions (ORION)	Durvalumab ± olaparib	II	NCT03775486

[a]Externally sponsored research conducted by M.D. Anderson Cancer Center.

PARP inhibition

Olaparib

Tumor Types: Ovarian cancer, Breast cancer, Pancreatic cancer, Colorectal cancer, Prostate cancer, Endometrial cancer, Bladder cancer, Gastric cancer, NSCLC, and Advanced solid tumors

Clinical Trial Information

Tumor	Setting	Regimen	Phase	Trial identifier
Endometrial cancer	Advanced and recurrent endometrial cancer (DUO-E)	Durvalumab ± olaparib	III	NCT04269200
Bladder cancer	Urinary bladder neoplasms, cisplatin-ineligible (BAYOU)	Durvalumab ± olaparib	II	NCT03459846
Advanced solid tumors	Advanced solid tumors (MEDIOLA)	Olaparib + durvalumab	I/II	NCT02734004
	Solid tumors in pediatric patients	Olaparib	I	NCT04236414
	Advanced solid tumors	AZD7648 Olaparib ± AZD7648 AZD7648 ± pegylated liposomal doxorubicin (PLD)	I/II	NCT03907969
Prostate Cancer	Metastatic castration-resistant (PROPel)	Olaparib + abiraterone	III	NCT03732820
	High-risk biochemically recurrent	Olaparib	II	NCT03047135[a]
	Metastatic castration-resistant (PROfound)	Olaparib vs. enzalutamide/abiraterone acetate	III	NCT02987543
	Metastatic castration-resistant	Olaparib, abiraterone acetate, prednisone	II	NCT03012321[b]
	HRRm metastatic castration-resistant	Olaparib, abiraterone acetate, prednisone	II	NCT01972217
	Castration-resistant	Olaparib + testosterone	II	NCT03516812[c]
Advanced cancers	BRCA or ATM mutations (TAPUR)	Abemaciclib, afatinib, talazoparib, crizotinib, palbociclib, sunitinib, temsirolimus, trastuzumab + pertuzumab, vemurafenib + cobimetinib, dasatinib, regorafenib, olaparib, pembrolizumab, nivolumab + ipilimumab	II	NCT02693535[d]

[a]Externally sponsored research conducted by Sidney Kimmel Comprehensive Cancer Center at John Hopkins; [b]Externally sponsored research conducted by Northwestern University; [c]Externally sponsored research conducted by University of Washington and co-sponsored by National Cancer Institute; [d]Externally sponsored research conducted by American Society of Clinical Oncology.

PARP inhibition

Olaparib

Tumor Types: Ovarian cancer, Breast cancer, Pancreatic cancer, Colorectal cancer, Prostate cancer, Endometrial cancer, Bladder cancer, Gastric cancer, NSCLC, and Advanced solid tumors

References

1. Underhill C, Toulmonde M, Bonnefoi H. *Ann Oncol*. 2011;22(2):268-279.
2. Yelamos J, Farres J, Llacuna L, et al. *Am J Cancer Res*. 2011;1(3):328-346.
3. Noel C, Pawel JW, Boris A, et al. *J Clin Oncol*. 2018;36(suppl 15):5003.

PARP inhibition

Olaparib

Tumor Types: Ovarian cancer, Breast cancer, Pancreatic cancer, Colorectal cancer, Prostate cancer, Endometrial cancer, Bladder cancer, Gastric cancer, NSCLC, and Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

BRCA	Breast cancer gene	**HRR**	Homologous recombination repair
NAD	Nicotinamide adenine dinucleotide	**PLD**	Phospholipase D
ADP	Adenosine diphosphate	**HRRm**	Homologous recombination repair mutation
EGFR	Epidermal growth factor receptor	**NSCLC**	Non-small-cell lung cancer
ALK	Anaplastic lymphoma kinase		

WEE1 kinase inhibition

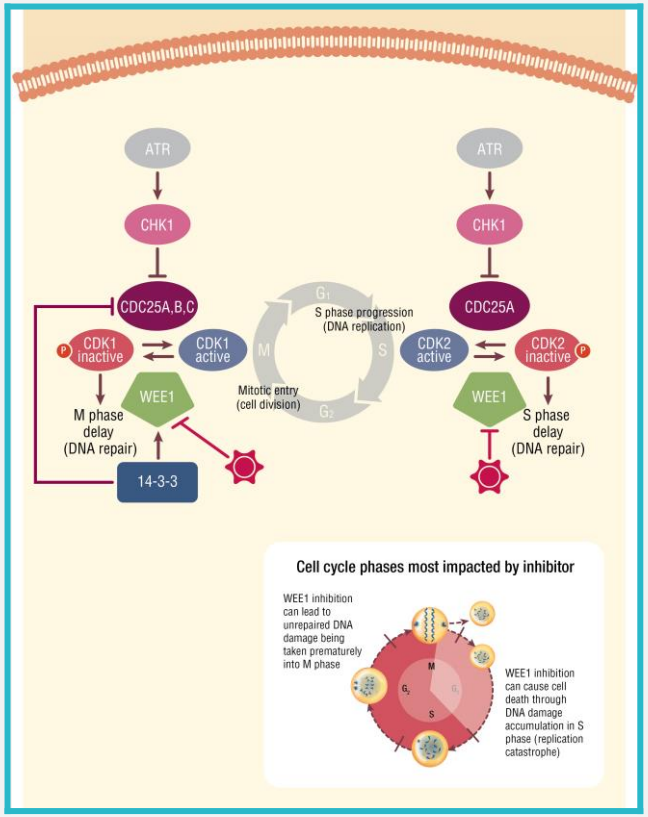
Adavosertib (AZD1775)

Tumor Types: SCLC, Solid tumors, and Bladder cancer

Target Overview

WEE1 is a cell cycle checkpoint kinase that regulates cell cycle progression by phosphorylating and inhibiting the activity of cyclin-dependent kinases (CDKs). CDK1/2 activity is essential for progression through the cell cycle. WEE1-mediated inhibition of CDK1 activity establishes the G2/M DNA damage-induced cell cycle checkpoint.[1] WEE1 also phosphorylates CDK2 during S phase to ensure faithful completion of DNA replication.[1]

The high prevalence of genetic aberrations that deregulate the G1/S cell cycle transition seen in many cancers can cause replication stress and DNA damage in the S phase.[2,3] This leads to dependency on the WEE1-mediated G2/M DNA damage checkpoint to allow DNA damage repair before mitosis and cell division.[2,3]



WEE1 kinase inhibition

Adavosertib (AZD1775)

Tumor Types: SCLC, Solid tumors, and Bladder cancer

Compound Overview

Adavosertib[a] is a potent selective inhibitor of WEE1 that deregulates CDK1 and CDK2 activity, leading to accumulation of DNA damage in S phase and abrogation of the G2/M DNA damage checkpoint.[4,5]

Adavosertib is under investigation as a monotherapy in cancers with high replication stress and in combination with chemotherapy and other agents.

[a]Previously known as AZD1775, in-licensed from Merck & Co., Inc. (MSD).

DNA Damage Response

Exploiting pathway dependencies to potentially induce cancer death

WEE1 kinase inhibition

Adavosertib (AZD1775)

Tumor Types: SCLC, Solid tumors, and Bladder cancer

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Platinum refractory extensive-stage SCLC (BALTIC)	Adavosertib + carboplatin, durvalumab + tremelimumab, ceralasertib + Olaparib	II	NCT02937818
Muscle invasive bladder cancer (BISCAY)	Adavosertib + durvalumab (Module C)	I	NCT02546661

WEE1 kinase inhibition

Adavosertib (AZD1775)

Tumor Types: SCLC, Solid tumors, and Bladder cancer

References

1. Otto T, Sicinski P. *Nat Rev Cancer.* 2017;17(2):93-115.
2. Gaillard H, García-Muse T, Aguilera A. *Nat Rev Cancer*. 2015;15(5):276-289.
3. Mazouzi A, Velimezi G, Loizou J. *Exp Cell Res*. 2014;329(1):85-93.
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WEE1 kinase inhibition

Adavosertib (AZD1775)

Tumor Types: SCLC, Solid tumors, and Bladder cancer

Abbreviations

View all abbreviations & acronyms

ATR	Ataxia telangiectasia and Rad3-related protein	**CDC25**	Cell division control protein 25
CDK	Cyclin-dependent kinase	**G2**	Gap/growth phase II
CHK	Checkpoint kinase	**M**	Mitotic phase
G1	Gap/growth phase I	**SCLC**	Small-cell lung cancer
S	DNA synthesis (replication) phase		

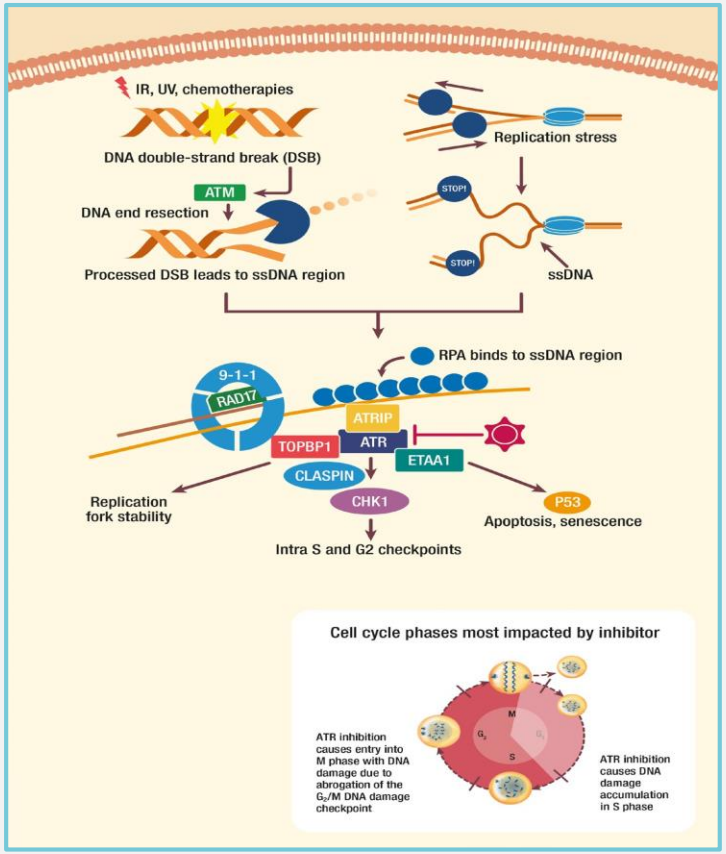
ATR kinase inhibition

Ceralasertib (AZD6738)

Tumor Types: Solid tumors and Hematologic malignancies, Breast, SCLC, Ovarian cancer, NSCLC, and HNSCC

Target Overview

- ATR, a serine/threonine protein kinase that is required for repair of stalled replication forks, is activated in response to double-strand breaks. It is a cell cycle checkpoint regulator.[1]
- ATR is a component of the Homologous Recombination Repair pathway
- Inhibition of ATR activity interferes with DNA damage responses and can lead to irreparable DNA damage, apoptosis, and hypersensitivity of tumors to replication-associated DNA-damaging agents.



ATR kinase inhibition

Ceralasertib (AZD6738)

Tumor Types: Solid tumors and Hematologic malignancies, Breast, SCLC, Ovarian cancer, NSCLC, and HNSCC

Compound Overview

Ceralasertib is a potent and selective oral ATR inhibitor[2] that is being clinically evaluated as a potential cancer treatment in advanced solid tumors and hematologic malignancies.

DNA Damage Response

Exploiting pathway dependencies to potentially induce cancer death

ATR kinase inhibition

Ceralasertib (AZD6738)

Tumor Types: Solid tumors and Hematologic malignancies, Breast, SCLC, Ovarian cancer, NSCLC, and HNSCC

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Refractory solid tumors	Ceralasertib	I/II	NCT02264678
Refractory solid tumors	Ceralasertib + carboplatin		
Refractory solid tumors, ATM-deficient and proficient gastric and gastroesophageal tumors, and BRCA mutated and non-mutated breast tumors	Ceralasertib + olaparib		
NSCLC, HNSCC	Ceralasertib + durvalumab		
Head and neck squamous cell cancer (biomarker window study)	Ceralasertib, olaparib	I	NCT03022409
Relapsed or refractory chronic lymphocytic leukemia (CLL)	Ceralasertib Ceralasertib + acalabrutinib	I/II	NCT03328273
Metastatic triple negative breast cancer stratified by BRCA1 or BRCA2 mutation (stratum A), mutation of other HRR pathway genes and no BRCA1 or BRCA2 mutation (stratum B), and no mutation of HRR genes (stratum C) (VIOLETTE)	Olaparib Olaparib + ceralasertib Olaparib + adavosertib	II	NCT03330847
NSCLC in patients who progressed on anti-PD-1/PD-L1 therapy (HUDSON)	Durvalumab + ceralasertib Durvalumab + danvatirsen Durvalumab + olaparib Durvalumab + oleclumab Durvalumab + cediranib Durvalumab + trastuzumab deruxtecan	II	NCT03334617

ATR kinase inhibition

Ceralasertib (AZD6738)

Tumor Types: Solid tumors and Hematologic malignancies, Breast, SCLC, Ovarian cancer, NSCLC, and HNSCC

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Relapsed/refractory Aggressive non-Hodgkin's lymphoma (PRISM Study)	AZD5153 + acalabrutinib AZD9150 + acalabrutinib Ceralasertib + acalabrutinib Hu5F9-G4 + rituximab + acalabrutinib	I	NCT03527147
Platinum refractory extensive-stage SCLC (BALTIC)	Ceralasertib + olaparib Durvalumab + tremelimumab Adavosertib + carboplatin (CBPT)	II	NCT02937818
Recurrent ovarian cancer (CAPRI)	Ceralasertib + olaparib	II	NCT03462342[a]
Platinum-sensitive relapsed epithelial ovarian cancer (DUETTE)	Olaparib Ceralasertib + olaparib	II	NCT04239014

[a]Externally sponsored research conducted by University of Pennsylvania.

ATR kinase inhibition

Ceralasertib (AZD6738)

Tumor Types: Solid tumors and Hematologic malignancies, Breast, SCLC, Ovarian cancer, NSCLC, and HNSCC

References

1. Yazinski SA, Zou L. *Annu Rev Genet.* 2016;50:155-173.
2. Foote KM, Lau A, Nissink JW. *Future Med Chem*. 2015;7(7):873-891.

ATR kinase inhibition

Ceralasertib (AZD6738)

Tumor Types: Solid tumors and Hematologic malignancies, Breast, SCLC, Ovarian cancer, NSCLC, and HNSCC

Abbreviations

View all abbreviations & acronyms

ATM	Ataxia telangiectasia mutated
ATR	Ataxia telangiectasia and rad 3-related
ATRIP	ATR interacting protein
BRCA 1/2	Breast cancer 1/2
CHK1	Checkpoint kinase 1
CLL	Chronic lymphocytic leukemia
ETAA1	Ewing's tumor-associated antigen 1
UV	Ultraviolet light
SCLC	Small cell lung cancer
PD-1	Programmed cell death-1
HNSCC	Head and neck squamous cell carcinoma
IR	Ionizing radiation
NSCLC	Non-small-cell lung cancer
9-1-1	RAD9-HUS1-RAD1 complex
RPA	Replication protein A
ssDNA	Single-strand DNA
TOPBP1	Topoisomerase binding protein 1
HRR	Homologous recombination repair
PD-L1	Programmed cell death ligand-1

AURKB inhibition

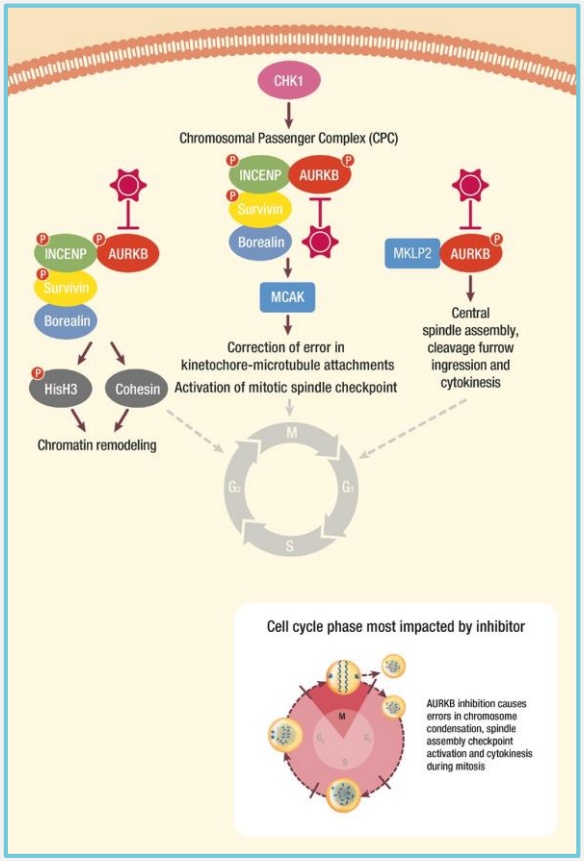
AZD2811 nanoparticle

Tumor Types: Solid tumors, SCLC, and Hematologic malignancies

Target Overview

AURKB, a member of a family of cell cycle proteins (AURKA, B, & C), regulates chromosome condensation, the spindle checkpoint, and cytokinesis during mitosis.[1-3] It is overexpressed in a variety of human solid tumors and several leukemias.

Inhibition of AURKB activity induces cell polyploidy, which may lead to apoptosis.[4]



AURKB inhibition

AZD2811 nanoparticle

Tumor Types: Solid tumors, SCLC, and Hematologic malignancies

Compound Overview

AZD2811 nanoparticle, an investigational potent and selective AURKB inhibitor, may induce tumor cell death in various solid[5] and hematologic tumors.[6] AZD2811 is the active component of prodrug AZD1152 (barasertib) encapsulated in a novel nanoparticle delivery system.[7]

DNA Damage Response

Exploiting pathway dependencies to potentially induce cancer death

AURKB inhibition

AZD2811 nanoparticle

Tumor Types: Solid tumors, SCLC, and Hematologic malignancies

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Acute myeloid leukemia/high-risk myelodysplastic syndrome	AZD2811 monotherapy AZD2811 + azacitidine AZD2811 + venetoclax AZD2811 + azacitidine + venetoclax	I/II	NCT03217838

AURKB inhibition

AZD2811 nanoparticle

Tumor Types: Solid tumors, SCLC, and Hematologic malignancies

References

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7. Song YH, Shin E, Wang H, et al. *J Control Release*. 2016;229:106-119.

AURKB inhibition

AZD2811 nanoparticle

Tumor Types: Solid tumors, SCLC, and Hematologic malignancies

Abbreviations

View all abbreviations & acronyms

AURKB	Aurora kinase B
CHK	Checkpoint kinase
G1	Gap/growth phase I
G2	Gap/growth phase II
HisH3	Histone H3
SCLC	Small-cell lung cancer
INCENP	Inner centromere protein
M	Mitotic phase
MCAK	Mitotic centromere-associated kinesin
MKLP2	Mitotic kinesin-like protein 2
S	DNA synthesis (replication) phase
CPC	Chromosome passenger complex

ATM inhibition

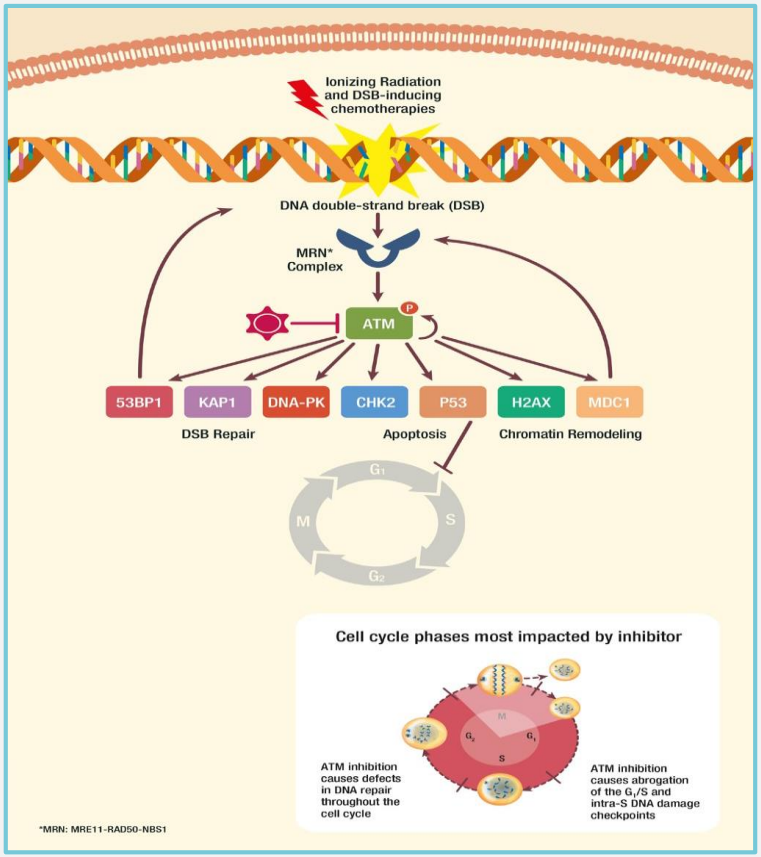
AZD1390

Tumor Types: CNS malignancies

Target Overview

ATM together with ATR and DNA-PK is 1 of 3 key serine/threonine PI3-kinase-like-protein-kinases involved in the DNA damage response.[1]

ATM specifically coordinates the signaling and repair of chromosomal DNA double-strand breaks. Accordingly, inhibition of ATM makes tumors hypersensitive to agents that lead to DSBs, such as chemotherapies, radiation therapy, and other inhibitors of the DNA damage response.[2,3]



ATM inhibition

AZD1390

Tumor Types: CNS malignancies

Compound Overview

AZD1390 is a potent and selective orally bioavailable ATM inhibitor that was specifically optimized for use in central nervous system malignancies. It is being investigated as a potential cancer treatment in advanced tumors.

DNA Damage Response

Exploiting pathway dependencies to potentially induce cancer death

ATM inhibition

AZD1390

Tumor Types: CNS malignancies

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Glioblastoma and CNS metastases from solid tumors	AZD1390 + radiotherapy	I	NCT03423628

ATM inhibition

AZD1390

Tumor Types: CNS malignancies

References

1. Durant ST et al. *Sci Adv*. 2018;4(6):eaat1719.
2. Shiloh Y, Ziv Y. *Nat Rev Mol Cell Biol*. 2013;14(4):197-210.
3. Blackford AN, Jackson SP. *Mol Cell*. 2017;66(6):801-817.

ATM inhibition

AZD1390

Tumor Types: CNS malignancies

Abbreviations

View all abbreviations & acronyms

53BP1	p53-binding protein 1
ATM	Ataxia telangiectasia mutated
ATR	Ataxia telangiectasia and rad 3-related
CHK	Checkpoint kinase
DNA-PK	DNA-dependent protein kinase
PI3	Peptidase Inhibitor 3
S	DNA synthesis (replication) phase
DSB	Double-strand break
H2AX	H2A histone family, member X
KAP1	Krüppel-associated box-associated protein 1
MDC1	Mediator of DNA damage checkpoint protein 1
CNS	Central nervous system
MRN	Mre11-Rad50-Nbs1
M	Mitotic phase

DNA-PK inhibition

AZD7648

Tumor Types: Advanced solid tumors

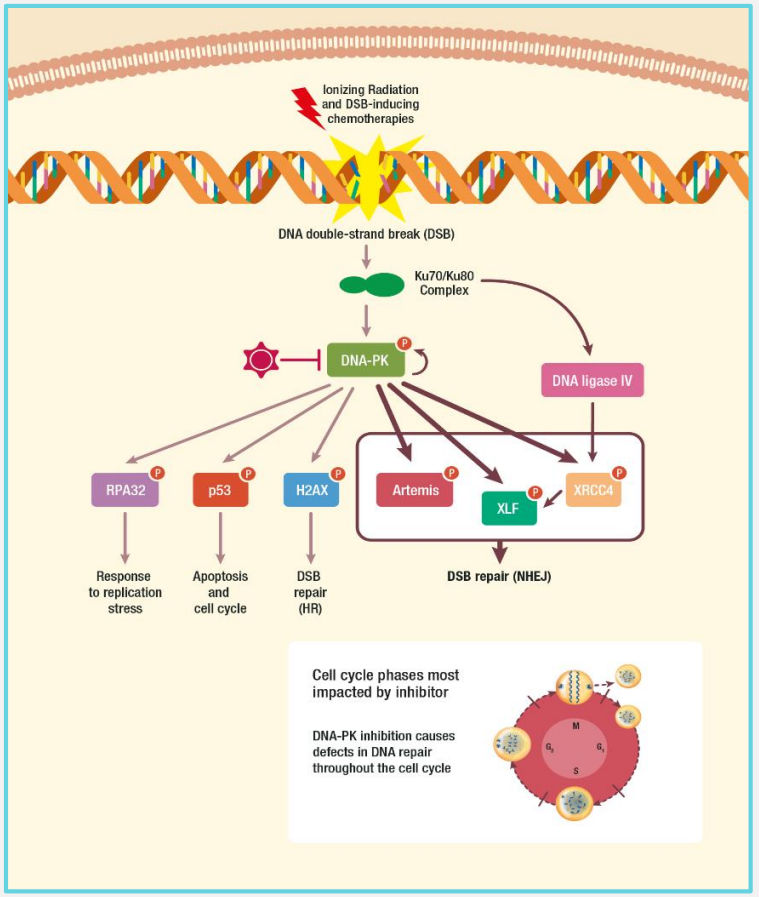
Target Overview

DNA-PK (DNA-dependent protein kinase) is a member of the PIKK (phosphatidylinositol 3-kinase-related kinase) family.[1]

DNA-PK is activated in response to DNA double-strand breaks (DSBs) via the NHEJ (non-homologous end joining) pathway.[1]

Inhibition of DNA-PK sensitizes to DSB-inducing agents such as chemotherapies, radiation therapy, and other inhibitors of the DNA damage response.[1]

DNA-PK has also been implicated in a range of other biologic processes, including modulation of chromatin structure, telomere maintenance, transcriptional regulation, and the response to replication stress.[2]



DNA-PK inhibition

AZD7648

Tumor Types: Advanced solid tumors

Compound Overview

AZD7648 is a potent selective inhibitor of DNA-PK that is being evaluated as a potential cancer treatment in advanced solid tumors.[3,4]

DNA Damage Response

Exploiting pathway dependencies to potentially induce cancer death

DNA-PK inhibition

AZD7648

Tumor Types: Advanced solid tumors

Clinical Trial Information

Tumor	Regimen	Phase	Trial identifier
Advanced malignancies	AZD7648 AZD7648 ± olaparib AZD7648 ± pegylated liposomal doxorubicin (PLD)	I/II	NCT03907969

DNA-PK inhibition

AZD7648

Tumor Types: Advanced solid tumors

References

1. Blackford AN, Jackson SP. *Mol Cell*. 2017;66(6):801-817.
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DNA-PK inhibition

AZD7648

Tumor Types: Advanced solid tumors

Abbreviations

View all abbreviations & acronyms

DNA-PK	DNA-dependent protein kinase	**XRCC4**	X-ray repair cross complementing protein 4
CHK2	Checkpoint kinase 2	**HR**	Homologous recombination
H2AX	H2A histone family member X	**NHEJ**	Non-homologous end joining
XLF	XRCC4-like factor	**DSB**	Double-strand break
PIKK	Phosphatidylinositol 3-kinase-related kinase	**RPA32**	Replication protein A 32

Anti-BCMA ADC

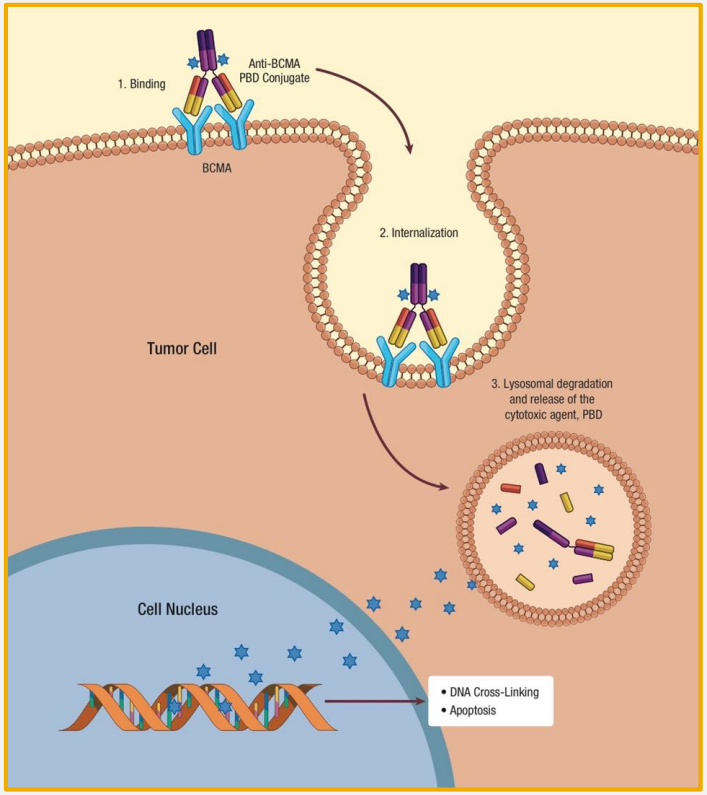
MEDI2228

Tumor Types: Relapsed/refractory multiple myeloma

Target Overview

BCMA is a cell surface receptor of the TNF receptor superfamily that is expressed in nearly all malignant T cells in multiple myeloma regardless of disease stage and genetic subtype.[1,2]

BCMA can be used as an antigen for ADC targeting due to its highly restricted normal tissue expression profile and its prevalence in multiple myeloma.[2,3]



Anti-BCMA ADC

MEDI2228

Tumor Types: Relapsed/refractory multiple myeloma

Compound Overview

MEDI2228 is an investigational ADC consisting of an anti-BCMA antibody site-specifically conjugated with a cytotoxic DNA cross-linking PBD dimer. The ADC preferentially binds to membrane-bound BCMA and is hypothesized to maintain activity in the presence of soluble BCMA.[4]

Once internalized, MEDI2228 releases the PBD dimer to cross-link DNA and trigger cell death in both multiple myeloma and multiple myeloma progenitor cells.[4]

MEDI2228 is being clinically evaluated as an anticancer treatment for relapsed/refractory multiple myeloma patients.

Antibody Drug Conjugates

Innovative approaches to selectively deliver cytotoxic payload to tumors

Anti-BCMA ADC

MEDI2228

Tumor Types: Relapsed/refractory multiple myeloma

Clinical Trial Information

Tumor	Regimen	Phase	Trial Identifier
Relapsed/refractory multiple myeloma	MEDI2228	I	NCT03489525

Anti-BCMA ADC

MEDI2228

Tumor Types: Relapsed/refractory multiple myeloma

References

1. Lee L, Bounds D, Paterson J, et al. *Br J Haematol*. 2016;174(6):911-922.
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4. Kinneer K, Meekin J, Varkey R, et al. *Blood.* 2017;130:3153.

Anti-BCMA ADC

MEDI2228

Tumor Types: Relapsed/refractory multiple myeloma

Abbreviations

View all abbreviations & acronyms

ADC	Antibody drug conjugate	**TNF**	Tumor necrosis factor
BCMA	B-cell maturation antigen	**PBD**	Pyrrolobenzodiazepine

Anti-HER2 ADC

Trastuzumab deruxtecan[a]

Tumor Types: Breast cancer, Advanced solid tumors, Colorectal cancer, Gastric cancer, NSCLC, and Bladder cancer

Target Overview

The human epidermal growth factor receptor 2 (HER2) is a transmembrane tyrosine kinase receptor located on chromosome 17q21. It is a member of the epidermal growth factor receptor (EGFR) family, which also includes EGFR (HER1), HER3, and HER4.[1]

In normal cells, activation of HER2 via homo- or heterodimerization mediates cell-signaling pathways, including the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR) and mitogen-activated protein kinase (MAPK) pathways, which regulate cellular processes of proliferation, motility, and survival.[1]

HER2 acts as an oncogene in cancer, its overexpression resulting in ligand-independent dimerization, which leads to constitutive activation of its cytoplasmic kinase domain. This constitutive activation of HER2 leads to unregulated activation of the PI3K/AKT/mTOR and MAPK pathways, which promotes uncontrolled cell proliferation, evasion of apoptosis, angiogenesis, and invasion, leading to tumor growth and progression.[1]

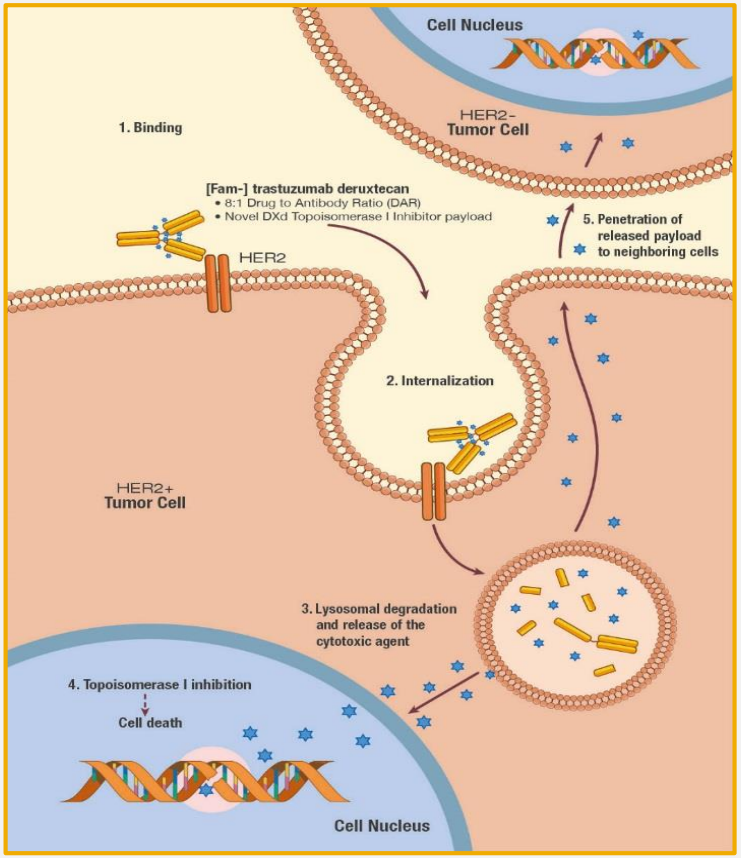

Figure adapted from Nakada T et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173-185.

[a]In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US.

Anti-HER2 ADC

Trastuzumab deruxtecan

Tumor Types: Breast, Advanced solid tumors, Colorectal, Gastric, NSCLC, and Bladder cancer

Compound Overview

Trastuzumab deruxtecan[a,b] is composed of a humanized anti-HER2 IgG1 monoclonal antibody with the same amino acid sequence as trastuzumab, covalently linked to a topoisomerase I inhibitor payload (an exatecan derivative) via a tetrapeptide-based cleavable linker. It is designed to target and deliver chemotherapy inside cancer cells that express HER2 and reduce systemic exposure to the cytotoxic payload compared to the way chemotherapy is commonly delivered.[2,3]

Based on in vitro and in vivo models, the released high cell-membrane payload DXd exerts antitumor activity through cytotoxic activity in both the target cells and neighboring tumor cells owing to the membrane permeability of the released cytotoxic payload.[2]

[a] fam-trastuzumab deruxtecan-nxki in US only; trastuzumab deruxtecan in other regions of world.
[b] In collaboration with Daiichi Sankyo Inc., Basking Ridge, NJ, US.

Antibody Drug Conjugates

Innovative approaches to selectively deliver cytotoxic payload to tumors

Anti-HER2 ADC

Trastuzumab deruxtecan

Tumor Types: Breast, Advanced solid tumors, Colorectal, Gastric, NSCLC, and Bladder cancer

Clinical Trial Information

Tumor	Regimen	Phase	Trial Identifier
Metastatic triple negative breast cancer (BEGONIA)	Durvalumab or capivasertib or oleclumab + paclitaxel or trastuzumab deruxtecan	II	NCT03742102
HER2+ unresectable and/or metastatic breast cancer (DESTINY-Breast01)	Trastuzumab deruxtecan	II	NCT03248492
HER2+ unresectable and/or metastatic breast cancer (DESTINY-Breast02)	Trastuzumab deruxtecan Capecitabine Lapatinib Trastuzumab	III	NCT03523585
HER2+ unresectable and/or metastatic breast cancer (DESTINY-Breast03)	Trastuzumab deruxtecan Ado-trastuzumab emtansine (T-DM1)	III	NCT03529110
HER2-low unresectable and/or metastatic breast cancer (DESTINY-Breast04)	Trastuzumab deruxtecan Capecitabine Eribulin Gemcitabine Paclitaxel Nab-paclitaxel	III	NCT03734029
HER2-low positive metastatic breast cancer (DESTINY-Breast06)	Trastuzumab deruxtecan Capecitabine Paclitaxel Nab-paclitaxel	III	NCT04494425
HER2-expressing unresectable and/or metastatic breast cancer	Trastuzumab deruxtecan	I	NCT03366428
HER2+ advanced and/or refractory gastric, gastroesophageal junction adenocarcinoma, or breast cancer	Trastuzumab deruxtecan	I	NCT03368196

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Clinical Trial Information

Tumor	Regimen	Phase	Trial Identifier
HER2+ advanced/metastatic gastric or GEJ adenocarcinoma (DESTINY-Gastric03)	Trastuzumab deruxtecan	II	NCT04379596
HER2+ unresectable or metastatic gastric or GEJ adenocarcinoma (DESTINY-Gastric02)	Trastuzumab deruxtecan	II	NCT04014075
HER2-expressing advanced gastric or GEJ adenocarcinoma (DESTINY-Gastric01)	Trastuzumab deruxtecan	II	NCT03329690
HER2-expressing advanced colorectal cancer	Trastuzumab deruxtecan	II	NCT03384940
HER2-expressing advanced colorectal cancer (DESTINY-CRC01)	Trastuzumab deruxtecan	II	NCT03384940
HER2-expressing advanced solid malignant tumors	Trastuzumab deruxtecan	I	NCT03383692
HER2-expressing solid and rare tumors (DESTINY-PanTumor02)	Trastuzumab deruxtecan	II	NCT04482309
HER2-expressing advanced breast and urothelial cancer	Trastuzumab deruxtecan + nivolumab	I/II	NCT03523572

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Clinical Trial Information

Tumor	Regimen	Phase	Trial Identifier
Locally advanced/metastatic NSCLC	Trastuzumab deruxtecan Pembrolizumab	I	NCT04042701
HER2-overexpressing or -mutated, unresectable and/or metastatic NSCLC (DESTINY-Lung01)	Trastuzumab deruxtecan	II	NCT03505710
Advanced solid tumors	Trastuzumab deruxtecan	I	NCT02564900
NSCLC in patients who progressed on anti-PD-1/PD-L1 therapy (HUDSON)	Durvalumab + ceralasertib Durvalumab + danvatirsen Durvalumab + olaparib Durvalumab + oleclumab Durvalumab + cediranib Durvalumab + trastuzumab deruxtecan	II	NCT03334617

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Anti-HER2 ADC

Trastuzumab deruxtecan

Tumor Types: Breast, Advanced solid tumors, Colorectal, Gastric, NSCLC, and Bladder cancer

Abbreviations

View all abbreviations & acronyms

ADC	Antibody drug conjugate
IgG1	Immunoglobulin G1
HER2	Human epidermal growth factor receptor 2
EGFR	Epidermal growth factor receptor
PI3K	Phosphatidylinositol 3-kinase
IgG1	Immunoglobulin G1
NSCLC	Non-small-cell lung cancer
GEJ	Gastroesophageal junction
MAPK	Mitogen-activated protein kinase
T-DXd	Trastuzumab deruxtecan
mTOR	Mammalian target of rapamycin

Abbreviations & Acronyms

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

#

1L	First line
2L	Second line
EIF4EBP1	Eukaryotic translation initiation factor 4E binding protein 1
53BPI	p53 binding protein 1
9-1-1	RAD9-HUS1-RAD1 complex

A

A2AR	Adenosine 2A receptor	**ATRIP**	ATR interacting protein
A2ARI	Adenosine 2A receptor inhibitor	**A2BR**	Adenosine 2B receptor
ABL	Abelson murine leukemia viral oncogene homolog	**ATM**	Ataxia telangiectasia mutated
ADC	Antibody drug conjugate	**ATP**	Adenosine triphosphate
AKT	Protein kinase B / also known as PKB	**ATR**	Ataxia telangiectasia and Rad-3 related
AML	Acute myeloid leukemia	**AURK**	Aurora kinase
AMP	Adenosine monophosphate	**ADP**	Adenosine diphosphate
ANG-2	Angiopoietin-2	**ALK**	Anaplastic lymphoma kinase
APC	Antigen-presenting cell	**ADCC**	Antibody-dependent cellular cytotoxicity

Abbreviations & Acronyms

B

BAK	BCL2-homologous antagonist/killer	**BRD4**	Bromodomain-containing protein 4
BAX	BCL2-associated X protein	**BET**	Bromodomain and extra-terminal domain
BCG	Bacille Calmette-Guerin (biologic)	**BRAF**	v-raf murine sarcoma viral oncogene homolog B1
BCMA	B-cell maturation antigen		
BCR	B-cell receptor		
BIM	BCL2-interacting mediator of cell death		
BLNK	B-cell linker		
BRCA	Breast cancer gene		
BTK	Bruton's tyrosine kinase		
BCL2	B-cell lymphoma 2		
BCLXL	B-cell lymphoma extra large		
BH3	BCL2 homology domain 3		
BID	BH3-interacting-domain death agonist		
BAD	BCLXL/BCL2-associated death promoter		
BTC	Biliary tract cancer		

Abbreviations & Acronyms

C

CD19	Cluster of differentiation 19	**Clb**	Chlorambucil
CD22	Cluster of differentiation 22	**CLL**	Chronic lymphocytic leukemia
CD28	Cluster of differentiation 28	**CNS**	Central nervous system
CD4	Cluster of differentiation 4	**CRPC**	Castration-resistant prostate cancer
CD39	Cluster of differentiation 39	**CPC**	Chromosomal passenger complex
CD40	Cluster of differentiation 40	**CDC24**	Cell division control protein 24
CD73	Cluster of differentiation 73	**CTL**	Cytotoxic T lymphocyte
CD8	Cluster of differentiation 8	**CTLA-4**	Cytotoxic T-lymphocyte antigen 4
CD80	Cluster of differentiation 80	**CXCL1**	Chemokine ligand 1
CD86	Cluster of differentiation 86	**CXCL8**	Chemokine ligand 8
Cdc	Cell-division cycle	**CXCR**	Chemokine receptor
CDK	Cyclin-dependent kinase	**CXCR2**	Chemokine receptor type 2
CDK9	Cyclin-dependent kinase 9	**CycT1**	Cyclin T1
CHK	Checkpoint kinase	**CT**	Chemotherapy
CHK1	Checkpoint kinase 1	**CRT**	Chemoradiotherapy
CHK2	Checkpoint kinase 2	**cMET**	Tyrosine-protein kinase Met

Abbreviations & Acronyms

D

DHAP	Dexamethasone, cytarabine, cisplatin
DLBCL	Diffuse large B-cell lymphoma
DLL4	Delta-like ligand 4
DNA	Deoxyribonucleic acid
DNA-PK	DNA-dependent protein kinase
DSB	Double-strand break
DEP®	Dendrimer drug delivery
DDR	DNA damage response
DAMPs	Damage-associated molecular patterns

E

EBRT	Extra Beam Radiotherapy
EGFR	Epidermal growth factor receptor
EGFRm	Epidermal growth factor receptor mutant
ER	Estrogen receptor
ERE	Estrogen response element
ERK	Extracellular signal-regulated kinase
ETAA1	Ewing's tumor-associated antigen 1

F

FAK	Focal adhesion kinase
FcγR	Fc-gamma receptor
FGF	Fibroblast growth factor
Flt1	Fms-related tyrosine kinase 1
Flt4	Fms-related tyrosine kinase 4
FOXO	Forkhead box protein O subclass
FADD	Fas-associated death domain
FGRS2	Fibroblast growth factor receptor substrate 2
FGFR	Fibroblast growth factor receptor
EGF	Epidermal growth factor
ERα	Estrogen receptor alpha

Abbreviations & Acronyms

G

G1 phase	Gap/growth phase I
G2 phase	Gap/growth phase II
GAB1	GRB2-associated binding protein 1 of 40 kDa
GAP	GTPase-activating protein
GEF	Guanine nucleotide exchange factor
GF	Growth factor
GITR	Glucocorticoid-induced tumor necrosis factor-related protein
GITR-L	Glucocorticoid-induced tumor necrosis factor-related protein ligand
GPCR	G protein coupled receptor
GRB2	Growth factor receptor-bound protein 2
GEJ	Gastroesophageal junction
G2/M	Gap/growth phase 2/cell division phase
G1/S	Gap/growth phase 1/DNA synthesis phase
GM-CSF	Granulocyte-macrophage colony-stimulating factor
GDP	Guanosine diphosphate
GTP	Guanosine triphosphate

H

H2AX	H2A histone family, member X
HCC	Hepatocellular carcinoma
HCL	Hairy cell leukemia
HER2	Human epidermal growth factor receptor 2
HGF	Hepatocyte growth factor
HisH3	Histone H3
HLA	Human leukocyte antigen
HLA-E	HLA class I histocompatibility antigen E
HNSCC	Head and neck squamous cell carcinoma
HPV	Human papillomavirus
HR	Homologous recombination
HSPG	Heparan sulfate proteoglycan
HRR	Homologous recombination repair
HRRm	Homologous recombination repair mutation

Abbreviations & Acronyms

ICE	Ifosfamide, carboplatin, etoposide
IFNα	Interferon alpha
IGF	Insulin-like growth factor
IGFR	Insulin-like growth factor receptor
IgG1λ	Immunoglobulin 1 lambda
IKK	I kappa B kinase
IL-12	Interleukin 12
ILR	Interleukin receptor
INCENP	Inner centromere protein
IR	Infrared
ISRE	Interferon stimulated response element
IT	Intratumoral
ITIM	Immunoreceptor tyrosine-based inhibition motif
I-Kb	Inhibitor of nuclear factor kappa B
IRF7	Interferon regulatory factor 7
IRAK	Interleukin-1 receptor associated kinase
IgG1	Immunoglobulin G1
IFN	Interferon
IO	Immuno oncology
LKB	Liver kinase B

J

JAK	Janus kinase

K

KAP1	Krüppel-associated box-associated protein 1
KDR	Kinase insert domain receptor

L

LIGIII	DNA ligase 3
LKB1	Liver kinase B1
LM	Leptomeningeal
LYN	Lck/Yes novel tyrosine kinase
LNP	Lipid Nanoparticle

Abbreviations & Acronyms

M

mRNA	Messenger RNA	**MSS-CRC**	Microsatellite stable colorectal cancer
M phase	Mitotic phase	**MEK**	Mitogen-activated protein/extracellular signal-regulated kinase
mAb	Monoclonal antibody	**MKLP2**	Mitotic kinesin-like protein 2
MAPK	Mitogen-activated protein kinase	**MHC**	Major histocompatibility complex
MCAK	Mitotic centromere-associated kinesin	**mLST8**	Mammalian target of rapamycin associated protein 8
MCL	Mantle cell lymphoma	**MM**	Multiple myeloma
MCL1	Myeloid cell leukemia 1	**mTOR**	Mammalian target of rapamycin
MCRPC	Metastatic castration-resistant prostate cancer	**mTORC**	Mammalian target of rapamycin complex
mDC	Myeloid dendritic cell	**MYC**	Myelocytomatosis viral oncogene
MDC1	Mediator of DNA damage checkpoint protein 1	**MYT1**	Myelin transcription factor 1
MDS	Myelodysplastic syndrome	**MKLP**	Mitotic kinesin-like protein

N

NAD	Nicotinamide adenine dinucleotide	**NKG2A**	Natural killer cell lectin-like receptor
NF-κB	Nuclear factor kappa-light chain enhancer of activated B-cells	**NHEJ**	Non-homologous end joining
NF1	Neurofibromatosis type I	**NSCLC**	Non-small-cell lung cancer
NFAT	Nuclear factor of activated T cells	**NDV**	Newcastle disease virus
NK	Natural killer	**NOXA**	Phorbol-12-myristate-13-acetate-induced protein 1
NIK	NF-κB inducing kinase		

Abbreviations & Acronyms

O

OX40L	OX40 ligand	**OXO40**	Tumor necrosis factor receptor superfamily member 4

P

p110	Catalytic subunit of PI3K	**PE38**	Pseudomonas exotoxin A (38KDa)
p85	Regulatory subunit of PI3K	**PI3K**	Phosphatidylinositol 3-kinase
PAK	p21 activated kinase	**PIGF**	Placental growth factor
PARG	Poly (ADP-ribose) glycohydrolase	**PIP2**	Phosphatidylinositol 4,5-bisphosphate
PARP	Poly (ADP-ribose) polymerase	**PIP3**	Phosphatidylinositol (3,4,5)-trisphosphate
PBD	Pyrrolobenzodiazepine	**PKC**	Protein kinase C
PD-1	Programmed cell death-1	**PNK**	Polynucleotide kinase 3-phosphatase
pDC	Plasmacytoid dendritic cell	**Pol I**	DNA polymerase beta
PD-L1	Programmed cell death ligand- 1	**Pol II**	RNA polymerase II
PD-L2	Programmed cell death ligand- 2	**PTEN**	Phosphatase and tensin homolog
PDK	Phosphoinositide-dependent kinase	**PUMA**	P53 upregulated modulator of apoptosis
PLCγ2	Phospholipase Cγ2	**PSMA**	Prostate-specific membrane antigen
PIP	Prolactin-induced protein	**P2X7**	P2X purinoreceptor 7
PI3	Peptidase Inhibitor 3	**PKA**	Protein kinase A
PIK3CB	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit beta	**PP2A**	Protein phosphatase 2

Abbreviations & Acronyms

P

PLC	Phospholipase C	**PTEFb**	Positive transcription elongation factor b
PLD	Phospholipase D	**P2Y2**	P2Y purinoreceptor 2
p53	Tumor suppressor protein	**PAMPs**	Pathogen-associated molecular pattern molecules
PIKK	Phosphatidylinositol 3-kinase-related kinases		

Abbreviations & Acronyms

R

R/R	Relapsed/refractory	**RheB**	Ras homolog enriched in brain
RAC	Ras-related c3 botulinum toxin substrate	**RPA**	Replication protein A
RAF	Rapidly accelerated fibrosarcoma	**RTK**	Receptor tyrosine kinase
RAS	Rat sarcoma	**R/R FL**	Relapsed /refractory follicular lymphoma
Rb	Retinoblastoma protein	**RPA32**	Replication protein 32

S

S phase	DNA replication phase	**SOS**	Son of sevenless
S6	Ribosomal subunit 6	**sqNSCLC**	Squamous non-small-cell lung cancer
S6K	S6 kinase	**SRC**	Rous sarcoma protein tyrosine kinase
SCLC	Small-cell lung cancer	**SSB**	Single-strand break
SERD	Selective estrogen receptor degrader	**ssDNA**	Single-strand DNA
SHC	Src homology 2 domain containing protein	**STAT**	Signal transducer and activator of transcription
SHP2	Src homology 2 domain phosphatase	**SYK**	Spleen tyrosine kinase
SoC	Standard of care		

Abbreviations & Acronyms

S

SHP1	Src homology region 2 domain-containing phosphatase-1	**SHIP**	Src homology 2 (SH2) domain containing inositol polyphosphate 5-phosphatase
SBRT	Stereotactic body radiation therapy	**SIVA**	Apoptosis-inducing factor
SCRT	Short course radiation therapy	**SERM**	Selective estrogen receptor modulator

Abbreviations & Acronyms

T

TCR	T-cell receptor
TK	Tyrosine kinase
TKI	Tyrosine kinase inhibitor
TLR 7/8	Toll-like receptor 7/8
TN	Treatment naïve
TNBC	Triple-negative breast cancer
TORC	Target of rapamycin complex
Treg	Regulatory T cell
TSC	Tuberous sclerosis complex
Tubulysin/ADC	Tubulysin antibody drug conjugate
TF	Tissue factor
TME	Tumor microenvironment
TRAF1	Tumor necrosis factor receptor-associated factor 1

U

UV	Ultraviolet
UC	Urothelial cancer

Z

ZAP70	Zeta-chain-associated protein kinase 70

V

VEGF	Vascular endothelial growth factor
VEGF-A	Vascular endothelial growth factor ligand A
VEGF-B	Vascular endothelial growth factor ligand B
VEGF-C	Vascular endothelial growth factor ligand C
VEGF-D	Vascular endothelial growth factor ligand D
VEGFR	Vascular endothelial growth factor receptor

W

WM	Waldenstrom's macroglobulinemia
Wnt	Wingless-related integration site
WT	Wild type

X

XRCC1	X-ray repair cross-complementing protein 1
XRCC4	X-ray repair cross-complementing protein 4
XLF	XRCC4-like factor

The information provided here regarding durvalumab, gefitinib, osimertinib, olaparib, selumetinib, and trastuzumab deruxtecan[a] are for uses that are currently under investigation. All other compounds are AstraZeneca investigational products still under development and, as such, are not approved by the US Food and Drug Administration, European Medicines Agency, or any other regulatory agency for the uses under investigation. Information regarding investigational products/indications should under no circumstances be regarded as a recommendation for their use or of their safety or efficacy.
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