AstraZeneca
What science can do

Hyatt Conference
Columbus2018

ASCO 2018 investor event; breakout 4: Next-gen Immuno-Oncology

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Three paths to improve the treatment of cancer

Examples

Introduce new SoC[1]

to create new treatment paradigm

- Phase III **PACIFIC** (Stage III NSCLC) ✓
- Phase III **ADJUVANT** (Stage I-III NSCLC)
- Phase III **POTOMAC** (NMI-UBC[3]) New

Replace SoC

to deliver longer OS[2]

- Phase III **MYSTIC** (Stage IV 1L NSCLC) ✗
- Phase III **PEARL** (Stage IV 1L NSCLC)
- Phase III **ARCTIC** (Sub-study B) (Stage IV 3L NSCLC) ✗
- Phase Ib **Study 1108** (Stage IV 2L UBC) ✓
- Phase III **DANUBE** (Stage IV 1L UBC)
- Phase III **HIMALYA** (Stage IV 1L HCC)
- Phase III **KESTREL** (Stage IV 1L HNSCC)

Add to SoC

to enable synergy or add activity

- Phase III **PACIFIC-2** (Stage III NSCLC) New
- Phase III **DUO-O** (Stage IV 1L ovarian) New
- Phase III **POSEDION** (Stage IV 1L NSCLC)
- Phase III **CASPIAN** (Stage IV 1L SCLC)

1. Standard of care.
2. Overall survival.
3. Non-muscle invasive urothelial bladder cancer.

Differentially invest, focus on early-stage, and unlock PD-L1/1-insensitive tumours

Differentially invest by tumour type

Lung:
Invest across all stages

Stage I/II	Stage III	Stage IV	PDx refractory

Ovarian:
1st-line indication with DUO-O

Stage I-III	1st line	PSR	PRR	4th line

Early-stage likely most IO-sensitive

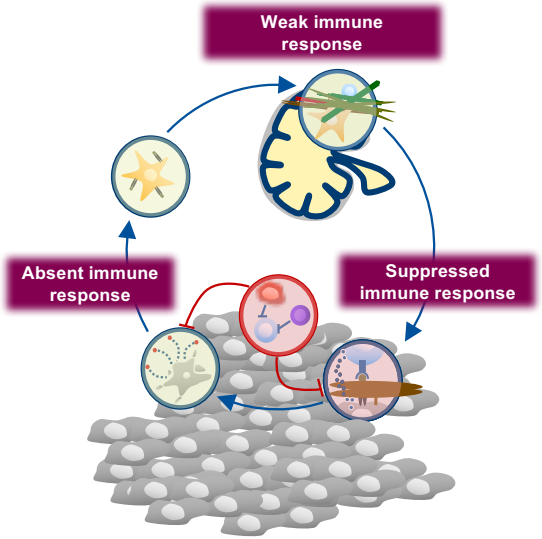
Stage I-III NSCLC
ADJUVANT, PACIFIC, PACIFIC-2

NMI-UBC
POTOMAC

Neo-adjuvant TNBC
GeparNuevo[1]

MIBC[2]
Gao et al.[3]

Unlock PDx-insensitive tumours with novel MOAs



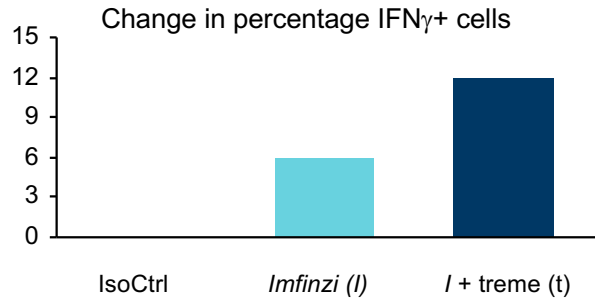
Examples of implementation

1. ASCO 2018 abstract 104.
2. MIBC = Muscle invasive bladder cancer.
3. ASCO 2018 ; abstract e16524.

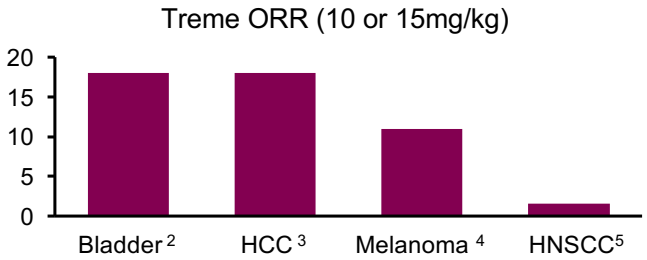
Exploring IO combinations: lessons from mono and combo

Which molecules?

Ex vivo TILs from NSCLC patients[1]

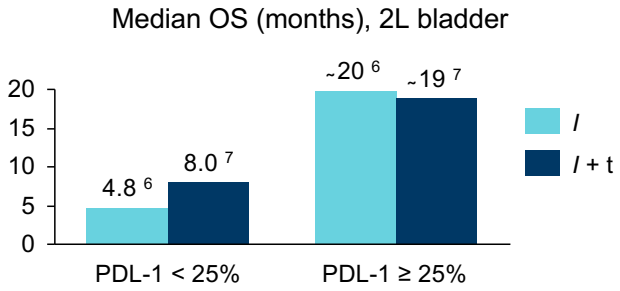


Monotherapy response



Who will benefit?

PD-L1 Immunohistochemistry



Novel predictive biomarkers

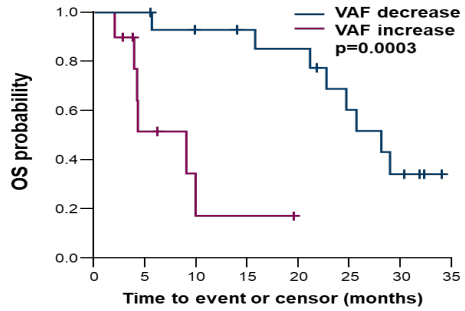
Tissue	Blood
IFNγ or phenomics	Expression or ctDNA
TMB	

How to study?

Platform trials

- Biomarker-selected
- Key indications
- Post-IO

Surrogate markers (i.e. ctDNA[8])

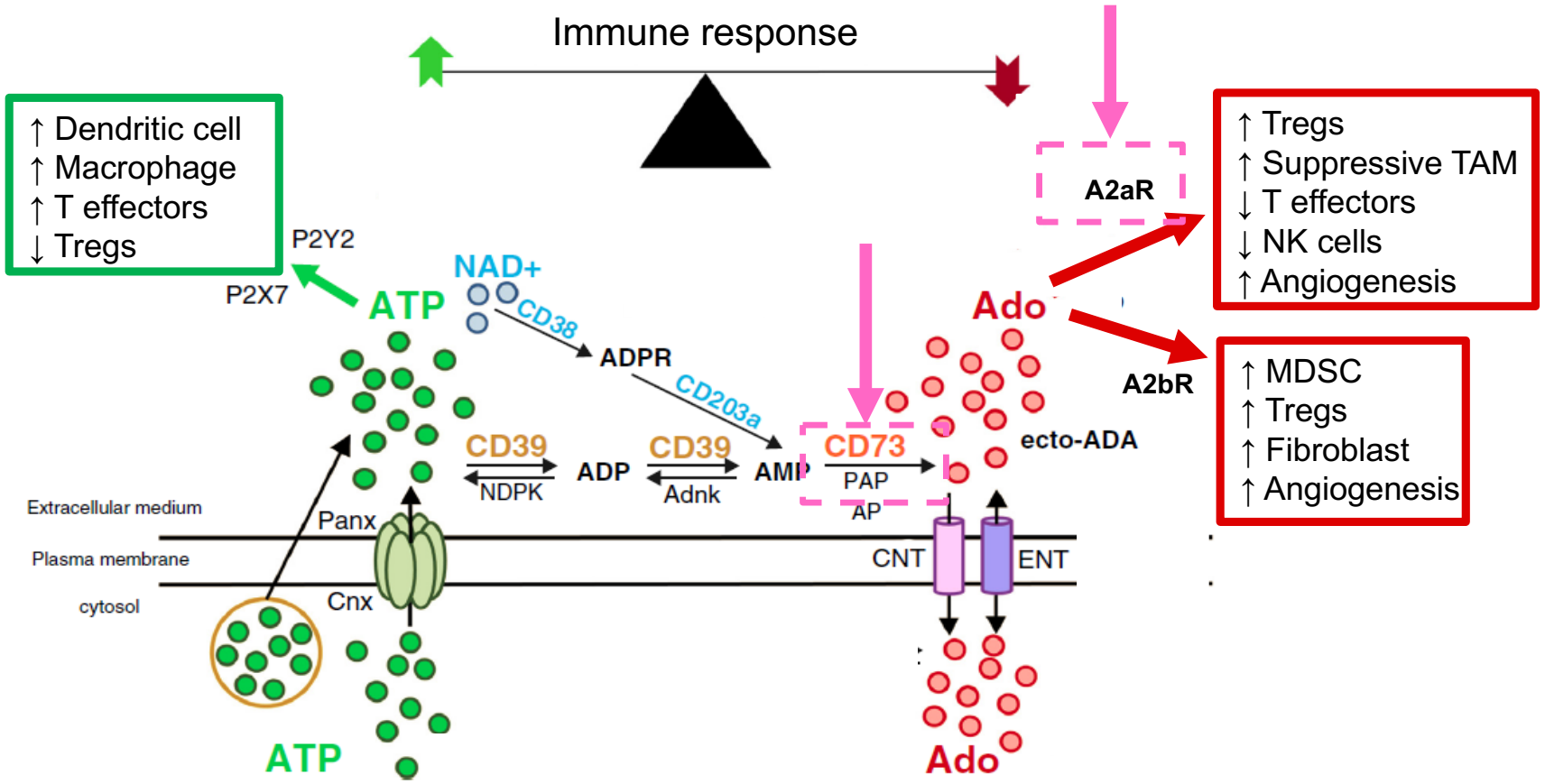


1. ASCO 2018 abstract 12104. 2. SITC 2017, abstract P213.
3. Sangro et. al. 2013. 4. Ribas et. al. 2013.
5. MHNCS 2018; IJRO vol 100; 5, page 1307.

6. AACR 2018, abstract CT031.
7. AACR 2018; abstract CT112.

8. AACR 2017; abstract 8518.

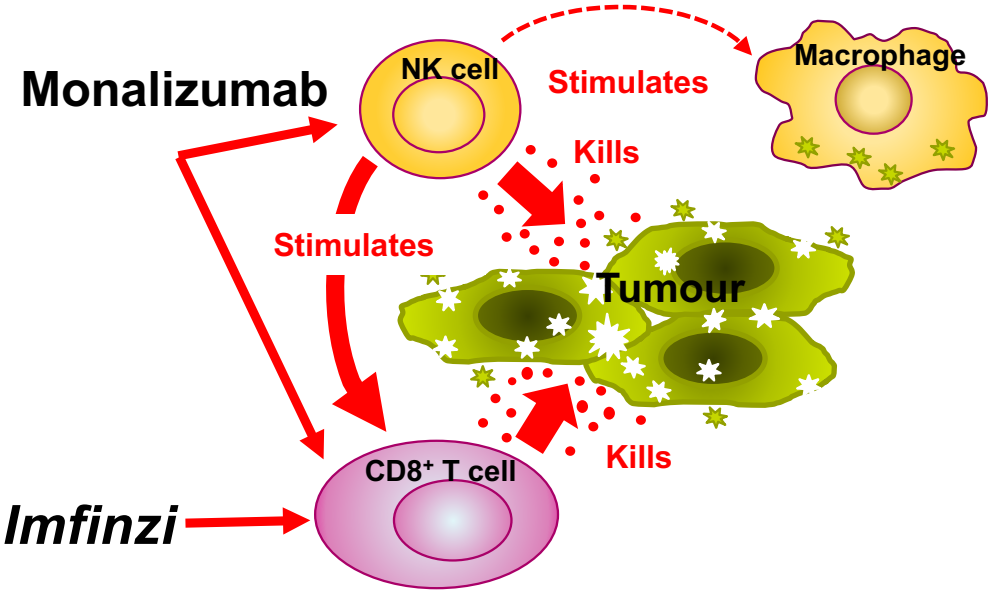
CD73 and A2aR are key players in the adenosine pathway and tumour microenvironment



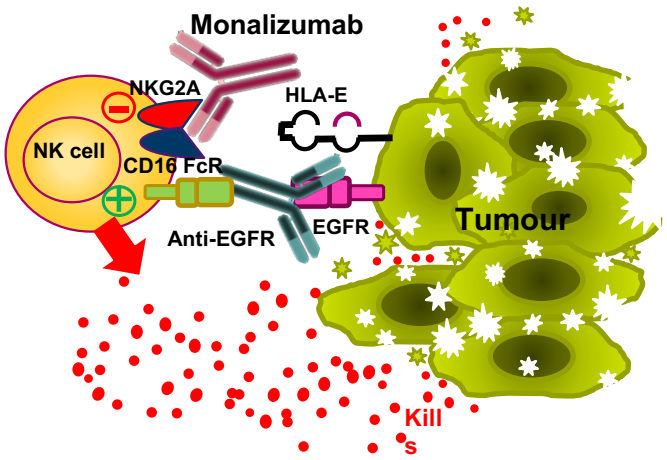
Source: Adapted from Allard, Curr Opin Parmacol (2016) 29:7.

Clinical development opportunities for monalizumab[1]

Hypothesis 1
Combination of non-redundant checkpoint pathways (monalizumab + *Imfinzi*) to enhance anti-tumor immunity



Hypothesis 2
Enhance NK cell dependent ADCC (monalizumab + ADCC-enabled antibody)



ADCC = antibody dependent cellular cytotoxicity.

Opportunities

Combination with *Imfinzi* in IO-insensitive tumours

Enhance ADCC

1. Monalizumab in partnership with Innate Pharma.

Q&A

Use of AstraZeneca conference call, webcast and presentation slides