
Roche

The next frontier in Cancer Immunotherapy

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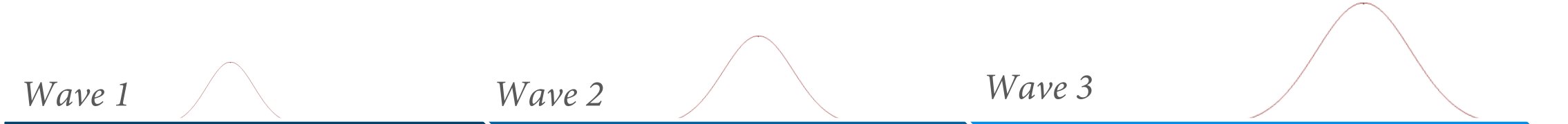
The state of cancer immunotherapy today



Monotherapy	Combine with SoC	CIT Combinations
• Durable responses have been observed in a subset of patients • Higher activity in “inflamed” tumor types (e.g. melanoma, bladder) or biomarker subpopulation (e.g. PD-L1+, MSI-H)	• CIT moving to earlier lines: first combination trials including chemotherapy and Avastin reading out throughout 2018 • Survival benefit has been observed in unselected patients, but may be enriched in some patients (e.g. PD-L1+, TMB high, T-eff high)	• Goal to expand breadth and depth of immune response • Novel agents aim to address specific immune escape mechanisms and individual patient biology

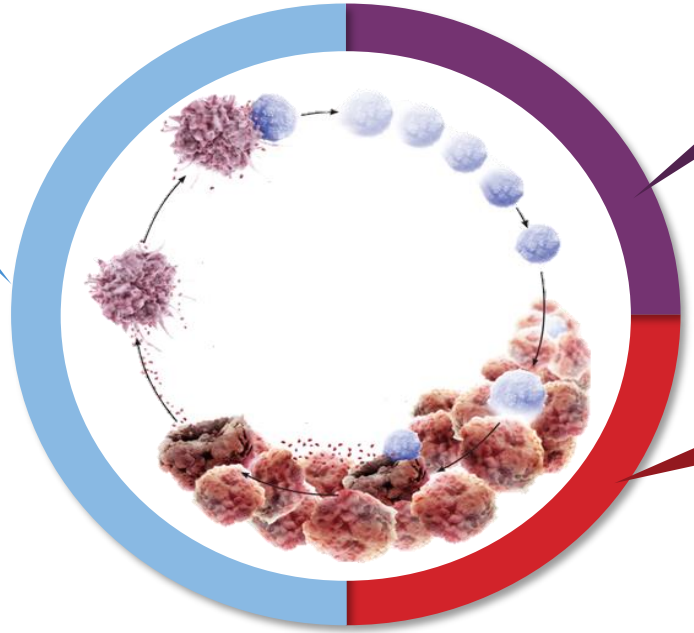
We are still in the early stages of unlocking the potential in cancer immunotherapy

TMB = Tumor Mutation Burden, SoC = Standard of Care, CIT = Cancer IMmunotherapy

Key strategies to reinitiate the antitumour immune response according to each phenotype

IMMUNE DESERT

- Generate/release/deliver antigens
- Enhance antigen presentation and T-cell priming
- Redirect and engage T cells



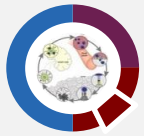
IMMUNE EXCLUDED

- Recruit T cells to tumour
- Address stromal barrier
- Redirect and engage T cells

INFLAMED

- Invigorate T cells
- Redirect and engage T cells

Some patients may only require targeting of negative regulator (aPD-L1 monotherapy) to enable cancer immunity



Some patients will need two or more therapies to enable cancer immunity (e.g., to drive infiltration, boost MHC expression, etc)

Adapted from Chen and Mellman. Immunity 2013; Hegde, et al. Clin Cancer Res 2016; Kim and Chen. Ann Oncol 2016; Chen and Mellman. Nature 2017

Investigating a diverse range of targets based on the characteristics of each immune phenotype

IMMUNE DESERT

TREATMENT STRATEGIES

Generate/release/deliver antigens

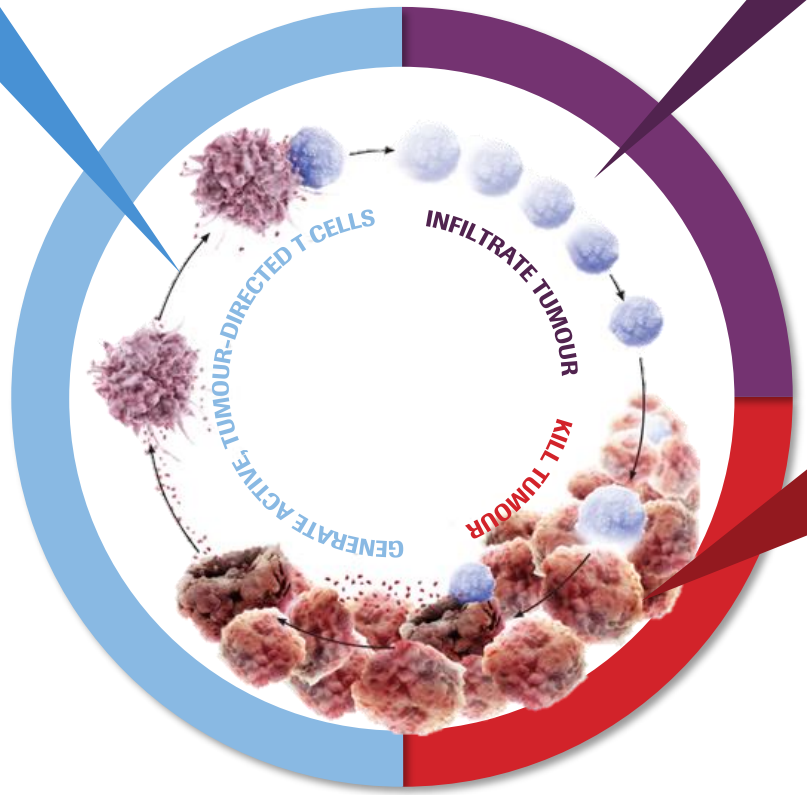
- Personalised cancer vaccine
- Vaccine*
- Oncolytic virus*
- CAR-T*
- Epigenetic modifiers (HDACi,* EZH2i*, DNMTi*)
- Immunogenic cell death (chemotherapy)*
- Radiotherapy*
- Targeted therapies: anti-HER2, BRAFi, EGFR-TKI, ALKi, PARPi*, anti-CD20, MEKi

Enhance antigen presentation and T-cell priming

- Anti-CD40
- Anti-CD27*

Redirect and engage T cells

- T-cell bispecifics (CEA-CD3 TCB, CD20-CD3 TCB, CD3-CD20 TDB)



IMMUNE EXCLUDED

TREATMENT STRATEGIES

Recruit T cells to tumour

- Anti-VEGF
- Anti-CXCR4*

Address stromal barrier

- Anti-stromal agent

Redirect and engage T cells

- T-cell bispecifics (CEA-CD3 TCB, CD20-CD3 TCB, CD3-CD20 TDB)

INFLAMED

TREATMENT STRATEGIES

Invigorate T cells

- Anti-PDL1
- Anti-VEGF
- MEKi
- IDOi
- Anti-OX40
- Anti-FAP-IL2v
- Anti-CEA-IL2v
- Anti-CSF1R
- Anti-TIGIT
- IDOi*
- Anti-A2A*
- Anti-CD38*

Redirect and engage T cells

- T-cell bispecifics (CEA-CD3 TCB, CD20-CD3 TCB, CD3-CD20 TDB)

*Clinical collaborations

Mapping of approaches to phenotypes based on current lead hypotheses

Does not preclude activity in other phenotypes

The information provided herein includes clinical data on non-approved indications for atezolizumab. As such, the efficacy and safety of atezolizumab in these indications has not been fully established

Adapted from Chen and Mellman. Immunity 2013; Hegde, et al. Clin Cancer Res 2016; Kim and Chen. Ann Oncol 2016; Chen and Mellman. Nature 2017

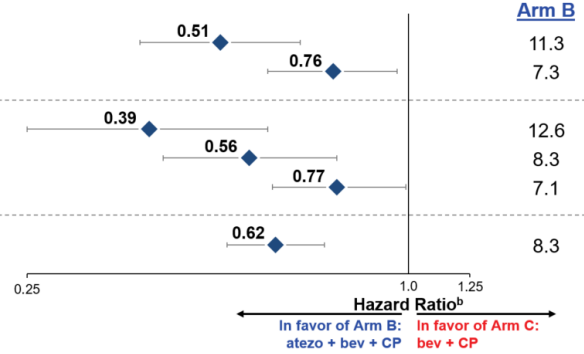
Tecentriq in 1L non-squamous NSCLC

IMpower150: A unique opportunity in key subgroups

FDA Priority Review (PDUFA Sep 5, 2018)

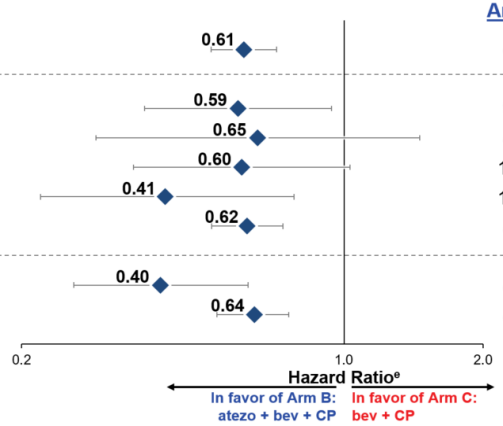
PDL-1 status (SP142 and SP263) and Teff signatures

Subgroup	n (%)[a]	Median PFS, mo Arm B	Arm C
Teff-high	284 (43%)	11.3	6.8
Teff-low	374 (57%)	7.3	7.0
PD-L1–High (TC3 or IC3)	135 (20%)	12.6	6.8
PD-L1–Low (TC1/2 or IC1/2)	224 (32%)	8.3	6.6
PD-L1–Negative (TC0 and IC0)	338 (49%)	7.1	6.9
ITT-WT	692 (100%)	8.3	6.8



EGFR/ALK genetic alterations and liver metastases

Populations	n (%)[a]	Median PFS, mo Arm B	Arm C
ITT (including *EGFR*/*ALK*+)	800 (100%)	8.3	6.8
EGFR/*ALK*+ only[b]	108 (14%)	9.7	6.1
ALK rearrangement[c]	34 (31%)	8.3	5.9
EGFR mutation[c]	80 (74%)	10.2	6.9
Exon 19 deletion or L858R[d]	59 (74%)	10.2	6.1
ITT-WT	692 (87%)	8.3	6.8
Liver metastases	110 (14%)	8.2	5.4
No liver metastases	690 (86%)	8.3	7.0

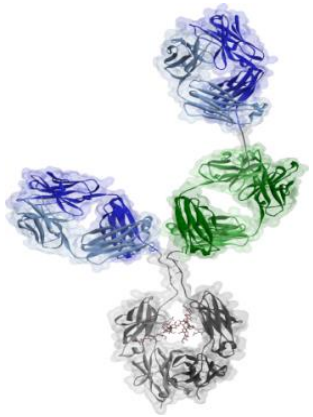


- **Strong ORR in ITT-WT: 64%**
- **Clinically meaningful PFS benefit in ITT and key subgroups (EGFR/ALK+ and patients with liver metastases)**
  - PD(L)1 monotherapy has not shown significant benefit in 2L EGFR/ALK+ patients
  - Tumors in patients with liver metastases are characterized by immune suppressive tumor environments, and they usually demonstrate poorer outcomes
  - The observed efficacy in these key subgroups may be due to the addition of Avastin to Tecentriq
- **Overall Survival data to be presented at ASCO 2018**

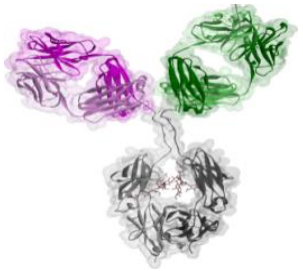
Kowanetz M, et al., AACR 2018; ITT=intent-to-treat; WT=wild type; mPFS=median progression free survival; TC=tumor cells; IC=immune cells; ORR = Overall Response Rate

Wave 3: novel combinations in cancer immunotherapy

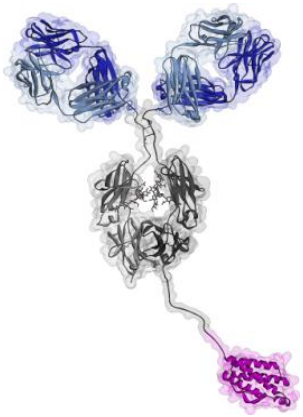
Roche CIT pipeline includes differentiated therapeutic platforms



CEA-CD3
CD20-CD3



CD20-CD3
FcRH5-CD3



CEA-IL2v
FAP-IL2v

PCV

Engage and activate T cells to kill tumour cells

Amplify immune response by delivery of tumour-targeted recombinant immunocytokine (IL-2)

Use a patient's unique neo-antigens to induce an antitumour immune response

PCV = Personalized Cancer Vaccine, CIT = Cancer Immunotherapy

ASCO 2018: Highlights in various cancer types*

June 1-5, 2018
McCormick Place | Chicago, IL
#ASCO18

Lung

- **Tecentriq + cb/pac +/- Avastin:** Ph III OS (*IMpower150*) in 1L non-squamous NSCLC
- **Tecentriq + cb + pac/nab-pac:** Ph III PFS (*IMpower131*) in 1L squamous NSCLC
- **Alecensa:** Ph III update (*ALEX*) in 1L ALK+ NSCLC

Hepatocellular carcinoma

- **Tecentriq + Avastin:** Ph Ib expansion (*GO30140*) in HCC

Breast

- **Ipatasertib:** Ph II (*LOTUS*) in 1L TNBC

Biomarker development

- **Tecentriq:** Ph II interim analysis (B-F1RST) to support blood TMB as predictive biomarker
- **Tecentriq:** Tissue TMB as predictive biomarker in NSCLC, mUC and melanoma

Hematology

- **Venclexta + Rituxan:** Ph III (*MURANO*) MRD analysis in R/R CLL
- **Venclexta + dec/aza:** Ph Ib (*NCT02203773*) in 1L AML
- **Venclexta + car + dex:** Ph II (*NCT02899052*) in R/R MM

*Planned submissions (to be confirmed); Outcome studies are event driven, timelines may change; cb=carboplatin; pac=paclitaxel; nab-pac=nab-paclitaxel (Abraxane); TMB= tumor mutational burden; aza=azacitidine; dec=decitabine; car=carfilzomib; dex=dexamethasone; Alecensa in collaboration with Chugai; Venclexta in collaboration with AbbVie

Doing now what patients need next