The next frontier in Cancer Immunotherapy

Daniel S. Chen, MD PhD
Vice President, Global Head of Cancer Immunotherapy

May 15, 2018
This presentation contains certain forward-looking statements. These forward-looking statements may be identified by words such as ‘believes’, ‘expects’, ‘anticipates’, ‘projects’, ‘intends’, ‘should’, ‘seeks’, ‘estimates’, ‘future’ or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this presentation, among others:

1. pricing and product initiatives of competitors;
2. legislative and regulatory developments and economic conditions;
3. delay or inability in obtaining regulatory approvals or bringing products to market;
4. fluctuations in currency exchange rates and general financial market conditions;
5. uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
6. increased government pricing pressures;
7. interruptions in production;
8. loss of or inability to obtain adequate protection for intellectual property rights;
9. litigation;
10. loss of key executives or other employees; and
11. adverse publicity and news coverage.

Any statements regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche’s earnings or earnings per share for this year or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

For marketed products discussed in this presentation, please see full prescribing information on our website www.roche.com

All mentioned trademarks are legally protected.
# The state of cancer immunotherapy today

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

<table>
<thead>
<tr>
<th>Wave 1</th>
<th>Wave 2</th>
<th>Wave 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monotherapy</strong></td>
<td><strong>Combine with SoC</strong></td>
<td><strong>CIT Combinations</strong></td>
</tr>
<tr>
<td>• Durable responses have been observed in a subset of patients</td>
<td>• CIT moving to earlier lines: first combination trials including chemotherapy and Avastin reading out throughout 2018</td>
<td>• Goal to expand breadth and depth of immune response</td>
</tr>
<tr>
<td>• Higher activity in “inflamed” tumor types (e.g. melanoma, bladder) or biomarker subpopulation (e.g. PD-L1+, MSI-H)</td>
<td>• Survival benefit has been observed in unselected patients, but may be enriched in some patients (e.g. PD-L1+, TMB high, T-eff high)</td>
<td>• Novel agents aim to address specific immune escape mechanisms and individual patient biology</td>
</tr>
</tbody>
</table>

**Key Points:**
- Durable responses observed in a subset of patients.
- Higher activity in “inflamed” tumor types or specific biomarker subpopulations.
- Citancer moving to earlier lines with combination trials.
- Survival benefits observed in unselected patients, potentially enriched in specific subgroups.
- Goal to expand immune response breadth and depth.
- Novel agents aim to address immune escape mechanisms.

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).

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)

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)

*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

Tecentriq in 1L non-squamous NSCLC

**IMpower150: A unique opportunity in key subgroups**

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

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)</th>
<th>Median PFS, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teff-high</td>
<td>284 (43%)</td>
<td>Arm B 11.3, Arm C 6.8</td>
</tr>
<tr>
<td>Teff-low</td>
<td>374 (57%)</td>
<td>Arm B 7.3, Arm C 7.0</td>
</tr>
<tr>
<td>PD-L1-High (TC3 or IC3)</td>
<td>135 (20%)</td>
<td>Arm B 12.6, Arm C 6.8</td>
</tr>
<tr>
<td>PD-L1-Low (TC1/2 or IC1/2)</td>
<td>224 (32%)</td>
<td>Arm B 8.3, Arm C 6.6</td>
</tr>
<tr>
<td>PD-L1-Negative (TC0 and IC0)</td>
<td>338 (49%)</td>
<td>Arm B 7.1, Arm C 6.9</td>
</tr>
<tr>
<td>ITT-WT</td>
<td>662 (100%)</td>
<td>Arm B 8.3, Arm C 6.8</td>
</tr>
</tbody>
</table>

**EGFR/ALK genetic alterations and liver metastases**

<table>
<thead>
<tr>
<th>Populations</th>
<th>n (%)</th>
<th>Median PFS, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT (including EGFR/ALK+)</td>
<td>800 (100%)</td>
<td>Arm B 8.3, Arm C 6.8</td>
</tr>
<tr>
<td>EGFR/ALK+ only*</td>
<td>108 (14%)</td>
<td>Arm B 9.7, Arm C 6.1</td>
</tr>
<tr>
<td>ALK rearrangement†</td>
<td>34 (21%)</td>
<td>Arm B 8.3, Arm C 5.9</td>
</tr>
<tr>
<td>EGRF mutation†</td>
<td>80 (74%)</td>
<td>Arm B 10.2, Arm C 6.9</td>
</tr>
<tr>
<td>Exon 19 deletion or L858R²</td>
<td>59 (74%)</td>
<td>Arm B 10.2, Arm C 6.1</td>
</tr>
<tr>
<td>ITT-WT</td>
<td>692 (87%)</td>
<td>Arm B 8.3, Arm C 6.8</td>
</tr>
<tr>
<td>Liver metastases</td>
<td>110 (14%)</td>
<td>Arm B 8.2, Arm C 5.4</td>
</tr>
<tr>
<td>No liver metastases</td>
<td>690 (86%)</td>
<td>Arm B 8.3, Arm C 7.0</td>
</tr>
</tbody>
</table>

- **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
Engage and activate T cells to kill tumour cells

CD20-CD3
FcRH5-CD3

CEA-IL2v
FAP-IL2v
Amplify immune response by delivery of tumour-targeted recombinant immunocytokine (IL-2)

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

PCV = Personalized Cancer Vaccine, CIT = Cancer Immunotherapy
ASC0 2018: Highlights in various cancer types*

**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