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

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04 June 2018
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Three paths to improve the treatment of cancer

**Introduce new SoC**
- to create new treatment paradigm

**Replace SoC**
- to deliver longer OS

**Add to SoC**
- to enable synergy or add activity

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

**Differentially invest by tumour type**

**Early-stage likely most IO-sensitive**

**Unlock PDx-insensitive tumours with novel MOAs**

**Lung:**
Invest across all stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>I/II</th>
<th>III</th>
<th>IV</th>
<th>PDx refractory</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I-III NSCLC</strong></td>
<td>ADJUVANT, PACIFIC, PACIFIC-2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NMI-UBC</strong></td>
<td>POTOMAC</td>
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</table>

**Ovarian:**
1st-line indication with DUO-O

<table>
<thead>
<tr>
<th>Stage</th>
<th>I-III</th>
<th>1st line</th>
<th>PSR</th>
<th>PRR</th>
<th>4th line</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neo-adjuvant TNBC</strong></td>
<td>GeparNuevo¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MIBC²</strong></td>
<td>Gao et al.³</td>
<td></td>
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</tbody>
</table>

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

Examples of implementation
Exploring IO combinations: lessons from mono and combo

**Which molecules?**

<table>
<thead>
<tr>
<th>Ex vivo TILs from NSCLC patients&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in percentage IFN&lt;sub&gt;γ&lt;/sub&gt;+ cells</td>
</tr>
<tr>
<td>IsoCtrl</td>
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<td>0</td>
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**Who will benefit?**

<table>
<thead>
<tr>
<th>PD-L1 Immunohistochemistry</th>
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<tbody>
<tr>
<td>Median OS (months), 2L bladder</td>
</tr>
<tr>
<td>PDL-1 &lt; 25%</td>
</tr>
<tr>
<td>4.8&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>-20&lt;sup&gt;6&lt;/sup&gt;</td>
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**Monotherapy response**

<table>
<thead>
<tr>
<th>Treme ORR (10 or 15mg/kg)</th>
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<tbody>
<tr>
<td>Bladder&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>20</td>
</tr>
</tbody>
</table>

**Novel predictive biomarkers**

- **Tissue**
  - IFN<sub>γ</sub> or phenomics

- **Blood**
  - Expression or ctDNA
  - TMB

**How to study?**

- Platform trials
  - Biomarker-selected
  - Key indications
  - Post-IO

**Surrogate markers (i.e. ctDNA<sup>8</sup>)**

1. ASCO 2018 abstract 12104.
2. SITC 2017, abstract P213.
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

↑ Dendritic cell
↑ Macrophage
↑ T effectors
↓ Tregs
↑ MDSC
↑ Tregs
↑ Fibroblast
↑ Angiogenesis

Immune response

Clinical development opportunities for monalizumab

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
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