Access and value for combination (immuno)oncology therapy...the forest and the trees

Reg Waldeck, PhD
March 1, 2017
Agenda

• How to think about access & value for combination (immuno)oncology?
• Current payer management in (immuno)oncology (I-O) combination therapy
• Towards an actionable access-value oncology framework …
Disclaimer

The views expressed are my own and do not necessarily reflect the views of my employer, Celldex Therapeutics, Inc.
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• How to think about access & value for combination (immuno)oncology?
• Current payer management in (immuno)oncology combination therapy
• Towards an actionable access-value oncology framework …
Insights on Future Payer Initiatives within Oncology…

Source: Celldex-commissioned research with Ken Kendall, 2016.
## Payers are increasing contacts with prescribers when a combination therapy is prescribed

### Payer Contact In Past 12 Months To Switch Treatment

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>% Among Community-based Oncologists Who Use The Drugs For 10% Of Their Patients That They Deem To Be Clinically Eligible</th>
<th>Mean % of Time Prescriber is Contacted by a Payer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tafinlar + Mekinist (n=24*)</td>
<td>42% <strong>8%</strong> 50%</td>
<td>21%</td>
</tr>
<tr>
<td>Tafinlar monotherapy (n=5**)</td>
<td>60% <strong>40%</strong></td>
<td>38%</td>
</tr>
<tr>
<td>Opdivo monotherapy (n=25*)</td>
<td>40% <strong>16%</strong> 44%</td>
<td>16%</td>
</tr>
<tr>
<td>Zelboraf + Cotellic (n=8**)</td>
<td>38% <strong>25%</strong> 38%</td>
<td>32%</td>
</tr>
<tr>
<td>Keytruda monotherapy (n=15*)</td>
<td>60% <strong>7%</strong> 33%</td>
<td>19%</td>
</tr>
<tr>
<td>Zelboraf monotherapy (n=9**)</td>
<td>56% <strong>11%</strong> 33%</td>
<td>22%</td>
</tr>
<tr>
<td>Yervoy monotherapy (n=18*)</td>
<td>39% <strong>28%</strong> 33%</td>
<td>23%</td>
</tr>
<tr>
<td>Opdivo + Yervoy (n=14*)</td>
<td>36% <strong>64%</strong></td>
<td>38%</td>
</tr>
</tbody>
</table>

**Source:** Kantar Health; Oncologist Survey, 2016— Q331D How often has a payer contacted you to switch your treatment selection and how does this compare with 1 year ago? Caution: *Small base size; **Very small base size

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Approx. 36% of oncologists who encounter payer challenges to Opdivo+Yervoy are more reluctant to prescribe, as a result of these reimbursement challenges. Please select the best response. SINGLE SELECT

**Likelihood of Reducing Prescribing Due to Reimbursement Challenges**

% Among Community-Based Oncologists Who Use Opdivo™ monotherapy, Keytruda™ monotherapy, Yervoy™ monotherapy, Opdivo™ + Yervoy™, for their 20% Patients that they deem to be clinically eligible

- **Opdivo™ monotherapy** (n=25*): 12% Yes, 88% No, 0% Don’t know
- **Keytruda™ monotherapy** (n=15*): 13% Yes, 87% No, 0% Don’t know
- **Yervoy™ monotherapy** (n=18*): 22% Yes, 78% No, 0% Don’t know
- **Opdivo™ + Yervoy™** (n=14*): 36% Yes, 64% No, 0% Don’t know

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**Source:** Kantar Health; Oncologist Survey, 2016—Q331G. Are you less likely to prescribe [PIPE IN 331A RESPONSE] as a consequence of these reimbursement challenges? Please select the best response. SINGLE SELECT

*Caution: *Small base size; **Very small base size
I-O Combinations were the most likely to be switched with another product as a result of reimbursement challenges

**Estimated Prescribed Patients**

% Among Community-Based Oncologists who use Opdivo™ monotherapy, Keytruda™ monotherapy, Yervoy™ monotherapy, Opdivo™ + Yervoy™ for at least 10% of their patients that they seem to be clinically eligible

<table>
<thead>
<tr>
<th>Product</th>
<th>% Ultimately Receiving Product</th>
<th>n*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opdivo monotherapy</td>
<td>98%</td>
<td>33</td>
</tr>
<tr>
<td>Keytruda monotherapy</td>
<td>95%</td>
<td>29</td>
</tr>
<tr>
<td>Yervoy monotherapy</td>
<td>95%</td>
<td>26</td>
</tr>
<tr>
<td>Opdivo + Yervoy</td>
<td>89%</td>
<td>16</td>
</tr>
</tbody>
</table>

**The estimate is calculated based on number of times that a prescriber is contacted by the payer to switch the drug that has been written for a patient; and the outcome – if the prescription is changed to the payer’s recommended product or if the prescriber proceeds with his original choice.**

**Source:** Kantar Health: Oncologist Survey, 2016—Q331A. Which of the following drugs do you use for at least 10% of the patients that you deem to be clinically eligible? AND Q331D. How often has a payer contacted you to switch your treatment selection AND Q331F. What percent of the time have payer policies led you to change from [PIPE IN 331A RESPONSE] to another agent

**Caution:** *Small base size*

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It’s not easy…

Treat to progression (TTP)

‘Innate immunity’

Fixed dose combination FDC)

Oncology value framework

The “tail”

Partnering

Risk-sharing

NCCN*

Outcomes-based agreements

Dosing schedule

‘Induction-maintenance’

Oncology quality metrics

Novel I-O outcome measures

Immuo-oncology

Oncology care model

Value –based payments

Number of cycles

(i)RECIST

Access hurdles

Target population

National Drug Code (NDC)

Pricing pressures

Comparative Effectiveness Research (CER)

Duration of therapy (DoT)

Incidence/Prevalence

Indication-specific pricing

NCCN denotes National Comprehensive Cancer Network
A little better…

<table>
<thead>
<tr>
<th>Micro/Macro</th>
<th>Health Care System</th>
<th>Key HC Trends</th>
<th>Oncology-specific</th>
<th>I-O-specific</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macro</strong></td>
<td>Access hurdles</td>
<td>Financial Risk-sharing</td>
<td>Oncology combination therapy</td>
<td>I-O combination therapy</td>
</tr>
<tr>
<td></td>
<td>Pricing pressures</td>
<td>CER</td>
<td>Oncology care model</td>
<td></td>
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<tr>
<td></td>
<td>Conditional/Accelerated approval</td>
<td>Cost-effectiveness</td>
<td>NCCN</td>
<td></td>
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<td></td>
<td>Partnering</td>
<td>Indication-specific pricing</td>
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<td></td>
<td>Incidence/Prevalence</td>
<td>Outcomes-based agreements</td>
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<td></td>
<td>Oncology care model</td>
<td>Value-based payments</td>
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<td>Indication-specific pricing</td>
<td></td>
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<tr>
<td><strong>Micro</strong></td>
<td>NDC</td>
<td>Target population</td>
<td>The “tail”</td>
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<tr>
<td></td>
<td>FDC</td>
<td>Treat-to-progression</td>
<td>‘Induction-maintenance’</td>
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<tr>
<td></td>
<td></td>
<td>Oncology quality metrics</td>
<td>‘Innate immunity’</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Number of cycles</td>
<td>‘Mutational load’</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Dosing schedule</td>
<td>Novel I-O trial designs &amp; outcome measures</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Oncology value frameworks</td>
<td>(i)-RECIST</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>DoT</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RECIST</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Better still…

Can we afford it?
- Epi
- Actuarial risk
- Risk-sharing?

Pricing pressures
Incidence / prevalence
Outcomes agreements
Value-based payments
NDC
TTP
DoT
Number of cycles
Dosing schedule
Partnering
Oncology care model

What’s the value?
- How to measure?
  - OS, PFS, ORR?
- Median, LYG*, QALY?
- Societal benefit?

(I)CER
FDC
NCCN
Oncology value frameworks
Oncology quality metrics

Who benefits?
- Target population
- Treatment heterogeneity?
- Risk factors?
- External validity?

Target population
Access hurdles
Conditional/Accelerated approval
Indication-specific pricing
Immuno-oncology
Innate Immunity
Induction-maintenance
i-RECIST
The “tail”
Mutational load
Novel I-O trial designs/outcomes

*LYG denotes life-years gained, which can be shown to be equivalent to the difference in mean survival
Getting there... an example for dosing schedule and how it relates to: "Can we afford it?"

- Can we afford it?
  - Study Arms
    - Drug A1
    - Drug A2
    - Drug B
  - Budget Impact

- Dosing Schedule
  - Fixed # cycles
  - TTP
  - Induction

- Dosing parameters
  - Maintenance

- Stopping rules
  - Stopping rule X

Impacts Treatment Cost
- Per Label
- Real World

Example only
Getting there...an example for dosing schedule and how it relates to: “What’s the value?”

- Drug A1+A2
- Drug B
- Drug A1
- Drug A2

Typical combination study

ΔOS, Tail, ΔPFS, ΔORR, ΔQALY, etc

Payers would like to know what Arm 3 looks like, as well

In this example, DoT (A1 then A2) > DoT (A1+A2) > DoT B
I-O Survival…”Who benefits?”

FDA-AACR: Immuno-oncology Drug Development Workshop

Oct. 13-14, 2016 | 8 a.m. – 5 p.m.
Hyatt Regency Washington on Capitol Hill, Washington, D.C.

*Transcripts and presentation slides are now available.

The goal of this workshop was to develop a path forward for evaluating an immuno-oncology-focused nonclinical and clinical development paradigm. Ideally, this workshop would help redefine biological outcome measures and clinical endpoints, leading to innovative clinical trial designs and statistical methods in the development of immuno-oncology clinical trials.

Getting there...an example for dosing schedule and how it relates to: “Who benefits?”

- Predictive Risk factors?
- Treatment heterogeneity
- Different cohorts with different characteristics?

Example Schematic only

Drug A + Drug B
TTP

Drug B
TTP

Drug B
Stopping Rule

No Rx
<table>
<thead>
<tr>
<th><strong>Access and value of combination immuno(oncology): Where from here?</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Can we afford it?</strong></td>
</tr>
<tr>
<td>At the macro-level, this will require some <strong>exploration of novel pricing / reimbursement models</strong>, such as annuities and other potential constructs.</td>
</tr>
<tr>
<td>At the micro-level this entails how <strong>different potential dosing and administration schedules</strong>, stopping rules, etc may facilitate payment models.</td>
</tr>
<tr>
<td><strong>What’s the value?</strong></td>
</tr>
<tr>
<td>Will we get to a <strong>generally acceptable value construct</strong> (framework) in oncology?</td>
</tr>
<tr>
<td>Will the system require evidence of <strong>sequential vs combination use</strong> (and variants thereof?)</td>
</tr>
<tr>
<td><strong>Who benefits?</strong></td>
</tr>
<tr>
<td>The science and biostatistics of I-O is relatively new; <strong>some more progress is needed</strong> before we can answer this question (better)</td>
</tr>
<tr>
<td><strong>Real-world tracking of outcomes and resource utilization</strong> will prove beneficial to our understanding, of who benefits and how?</td>
</tr>
</tbody>
</table>

**Propelling the field forward in the above three categories will increase our understanding of access and value within Oncology**