Background

- Diagnostic devices have become crucial to identifying patients with specific biomarkers for targeted treatment due to an increased focus on personalized medicine in oncology.
- By selecting specific patient populations, targeted therapies studied with companion diagnostic devices (CDx) can demonstrate clinically significant improvements over therapies studied without such devices.
- The potential improvement in benefit versus risk profile may translate to faster approvals and shorter development time.
- For example, comparing time from IND filing to approval for the first FDA-approved PD-1 inhibitors, KEYTRUDA® was developed in 56 months with a CDx, versus OPDIVO® in 101 months without a CDx.
- Biomarker-based development strategies may be applied to accelerate drug development and improve patient access to innovative treatments.

Objective

- The purpose of this research is to evaluate the impact on FDA approval timelines when using companion diagnostic devices for patient selection in the drug development process, ultimately leading to improved patient access to new oncology treatments.

Method

- Data was collected using publicly available resources:
  - A list of targeted oncology drug approvals from May 2003 to July 2018 were analyzed
  - Outcomes Measures:
    - Time from IND filing date to initial FDA approval
    - Median time from IND filing date to initial FDA approval

Results

- $\overline{\text{Mean Time from IND Filing Date to Initial FDA Approval Date: 61 months}}$
- $\overline{\text{Median Time from IND Filing Date to Initial FDA Approval Date: 60 months}}$

- 150
- 200
- 250
- 300
- 0
- 5
- 10
- 15
- 20
- 25
- 30

<table>
<thead>
<tr>
<th>Diagnostic Status</th>
<th>N</th>
<th>Mean Time from IND Filing Date to Initial FDA Approval Date</th>
<th>Median Time from IND Filing Date to Initial FDA Approval Date</th>
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<tbody>
<tr>
<td>CDx</td>
<td>65</td>
<td>61 months</td>
<td>60 months</td>
</tr>
<tr>
<td>No CDx</td>
<td>65</td>
<td>96.24 months</td>
<td>86.5 months</td>
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- Inclusion Criteria:
  - If the IND filing date was not publicly available or if early clinical development was conducted outside the US
  - Chemotherapy drugs

- Exclusion Criteria:
  - The majority of drugs with CDx (65% or 15 of 23) were approved based on Phase 1 or 2 clinical data compared to drugs without CDx, which were approved mostly based on Phase 3 data (57% or 24 of 42)

- 87% (20 of 23) approved drugs with CDx were small molecules (TKIs)

- The most commonly targeted indication was NSCLC (7 of 23)

- Overall, 65 oncology drugs approved between May 2003 and July 2018 met the analysis criteria

- 35% (23 of 65) had a CDx requirement versus 65% (42 of 65) did not have a CDx requirement to identify patients based on biomarkers

- The median time from IND filing date to initial FDA approval is 67.48 months for drugs approved with CDx versus 96.24 months for drugs without CDx (95% CI: -47.92 to -9.60, p = 0.0039)

- The longest time from IND filing to approval was 28 months for TAGRISSO® for EGFR T790M positive NSCLC, which was developed with a CDx

- The majority of drugs with CDx (65% or 15 of 23) were approved based on earlier Phase 1 or 2 clinical data compared to drugs without CDx, which were approved mostly based on Phase 3 data (57% or 24 of 42)

Conclusions

- From the results, using a CDx to identify patients who potentially best respond to the studied drug can lead to an improvement in benefit versus risk profile
- Oncology drugs developed with CDx not only have faster average development time, but also can be approved by the FDA based on earlier preliminary data

- Identifying targetable biomarkers remains a need for the less common tumor types

- Further research will involve quantifying the financial impact associated with CDx by reducing time to approval and the effect on improved patient access and clinical outcomes

Limitations

- Limited sample size analyzed; only new targeted therapies were analyzed
- Impact of longer survival in certain types of cancers, such as CML, were not considered in the analysis of overall development timeline
- Regulatory policy changes, such as the introduction of Breakthrough Therapy designation by FDASIA in July 2012, could have impacted the approval timeline of the newer therapies

Acknowledgment Information

- The authors of this presentation have nothing to disclose.