Special Considerations for Cancer Drug Development in Older Adults

Eric H. Rubin, M.D.
Merck Research Laboratories
Disclosures

• Employee, Merck Research Laboratories
Background

- While age is not a surrogate for physiology, special considerations may be needed for enrollment and treatment of elderly patients in clinical trials.
- Oncology studies sponsored by Merck &Co. generally do not have an upper age limit for eligibility.
- Other eligibility criteria that could be limiting with regard to age:
  - Pembrolizumab studies - renal function eligibility: creatinine ≤ 1.5 X upper limit of normal or creatinine clearance/GFR ≥ 30 mL/min for patients with creatinine levels > 1.5 X institutional ULN.
- For immunotherapies, do older patients benefit?
  - Immune function, including T cells, reported to decline with age (e.g. Montecino-Rodriguez, et al., J Clin Invest, vol 123, p 958-965, 2013).
Analyses of older patients treated in pembrolizumab clinical trials

• Pharmacokinetics
• Safety
• Efficacy
Pembrolizumab clearance is similar among older and younger patients

- Population PK modeling using 1223 patients with melanoma or NSCLC treated with pembrolizumab in KN001, KN002, or KN006
- Age range 15-94
- No correlation between age and clearance (p=0.246)

Pembrolizumab safety is similar among older and younger melanoma and NSCLC patients

KN001, KN002, KN006 and KN010 melanoma and lung cancer subjects treated with pembrolizumab

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;65</th>
<th>65-74</th>
<th>75-84</th>
<th>≥85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1587</td>
<td>857</td>
<td>316</td>
<td>39</td>
</tr>
<tr>
<td>Drug-related AE (%)</td>
<td>73</td>
<td>73</td>
<td>77</td>
<td>79.5</td>
</tr>
<tr>
<td>Drug-related SAE (%)</td>
<td>9</td>
<td>11</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Discontinued due to drug-related AE (%)</td>
<td>4</td>
<td>6</td>
<td>8.5</td>
<td>3</td>
</tr>
</tbody>
</table>

- No category of AE was exacerbated in any age group by pembrolizumab
Pembrolizumab efficacy is similar among older and younger melanoma and NSCLC patients

**KN006** – advanced melanoma patients treated with pembrolizumab 10 mg/kg Q2W or Q3W vs ipilimumab

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;65 yr</th>
<th>65-74</th>
<th>75-84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>201, 209</td>
<td>105, 110</td>
<td>29,33</td>
</tr>
<tr>
<td>OS hazard ratio</td>
<td>0.69</td>
<td>0.76</td>
<td>0.78</td>
</tr>
</tbody>
</table>


**KN010** – previously treated NSCLC patients with PD-L1 IHC TPS ≥ 1% treated with pembrolizumab 2 mg/kg vs docetaxel

<table>
<thead>
<tr>
<th>Number of patients (docetaxel, pembrolizumab)</th>
<th>&lt;65 yr</th>
<th>65-74</th>
<th>75-84</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS hazard ratio</td>
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<td>0.76</td>
<td>0.78</td>
</tr>
</tbody>
</table>
Summary

• In pembrolizumab clinical studies involving melanoma and lung cancer patients, older patients exhibit similar pharmacokinetics, safety, and efficacy compared to younger patients
  – Data support enrollment of older patients on clinical trials with PD-1 inhibitors

• Are eligibility criteria hindering enrollment of older patients onto clinical trials, or are they not being offered or have access to clinical trials?