## 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

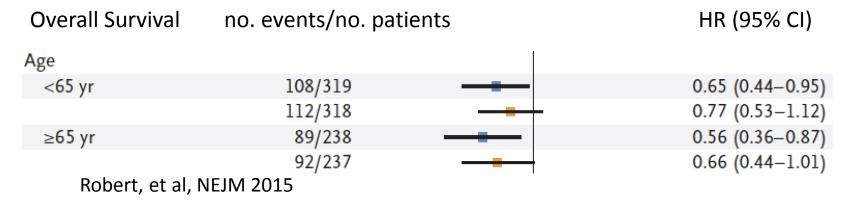
KN001, KN002, KN006 and KN010 melanoma and lung cancer subjects treated with pembrolizumab

Age	<65	65-74	75-84	≥85
Number of patients	1587	857	316	39
Drug-related AE (%)	73	73	77	79.5
Drug-related SAE (%)	9	11	13	10
Discontinued due to drug-related AE (%)	4	6	8.5	3

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



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

Age	<65	65-74	75-84
Number of patients (docetaxel, pembrolizumab)	201, 209	105, 110	29,33
OS hazard ratio	0.69	0.76	0.78

#### 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?