

# Special Considerations for Cancer Drug Development in Older Adults

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# 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  $\leq$  1.5 X upper limit of normal or creatinine clearance/GFR  $\geq$  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

Overall Survival	no. events/no. patients		HR (95% CI)	
Age	<65 yr	108/319		0.65 (0.44–0.95)
		112/318		0.77 (0.53–1.12)
	≥65 yr	89/238		0.56 (0.36–0.87)
		92/237		0.66 (0.44–1.01)

Robert, et al, NEJM 2015

KN010 – previously treated NSCLC patients with PD-L1 IHC TPS  $\geq$  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?