**Representativeness of Study Participants: Advanced Melanoma**

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| Considerations related to: |
| Sex | The incidence of melanoma of the skin is slightly higher in male versus female patients. Globally, the age-standardized rate of melanoma of the skin in 2020 was 3.8/100,000 for males and 3.0/100,000 for females.1  |
| Age | The risk of melanoma increases as people age. According to the American Cancer Society, the average age at which patients are diagnosed with melanoma is 65 years.2 Large-scale studies of patients with advanced melanoma that is resistant to anti-PD-1 therapy report a median age of 61–67 years at study enrolment.3,4 However, melanoma is not uncommon in younger individuals and is one of the most common cancers diagnosed in young adults.2 |
| Race/ethnicity | Melanoma is approximately 20-times more common in people of White versus African American ethnicity. The American Cancer Society reports the overall lifetime risk of being diagnosed with melanoma at approximately 2.6% (1 in 38), 0.1% (1 in 1,000), and 0.6% (1 in 167) for people of White, Black, and Hispanic ethnicity.2 |
| Geography | In 2020, the highest incidence of skin melanoma was reported in US (105,172 new cases), followed by Western Europe (65,168 new cases), and Northern Europe (33,551 new cases).1In 2020, age-standardized rates of skin melanoma were highest in Australia and New Zealand (35.8/100,000), Western Europe (18.9/100,000), Northern Europe (17.8/100,000), and US (16.1/100,000). In contrast, age-standardized rates of skin melanoma were markedly lower in Africa (e.g., Western Africa 0.48/100,000), Asia (e.g., Eastern Asia 0.39/100,000), and the Caribbean (0.70/100,000).1  |
| Other considerations | Cutaneous melanoma, arising in non-glabrous skin, is the most common subtype of melanoma. Acral melanoma is a distinct form originating in glabrous skin of the palms, soles, and nail beds. Uveal melanoma develops from melanocytes in the eyes, while mucosal melanoma, the rarest subtype, arises from melanocytes in the mucosal membranes.5 Melanomas are also further classified based on the occurrence of driver mutations, most notably *BRAF*-mutant, *NRAS*-mutant, *NF1*-loss and wild type, with *BRAF*-mutated disease being associated with particularly poor prognosis.5In large, randomized trials of immunotherapy for advanced melanoma, recruitment is generally focused on patients from Europe, US, Australia, and New Zealand.3,6 This is unsurprising, given these geographic regions comprise the majority of individuals diagnosed with melanoma.1 However, it is noteworthy that case fatality rates in US (0.07), Northern Europe (0.11), and Australia/New Zealand (0.08) are substantially lower than reported in other geographic regions including Western Africa (0.46), Caribbean (0.40), and South-Eastern Asia (0.50), suggesting a disparity in care.1 |
| Overall representativeness of this study | The patients recruited in our small pilot study included n=19, n=1, and n=1 of White, Black, and Asian ethnicity, respectively, broadly reflecting the incidence of melanoma reported in these populations. The distribution of male (n=11) and female (n=10) patients in our study reflects the slightly higher incidence of melanoma diagnoses in male versus female patients. The age distribution of patients in our study (median [range] 73 [40–87 years]) also broadly reflects that reported in other larger trials of patients with advanced melanoma resistant to anti-PD-1 therapy. While most patients in our study had cutaneous melanoma, the most commonly diagnosed subtype, individuals with acral and mucosal disease were also enrolled. Most patients had tumors with hallmark driver mutations in *BRAF*, *NRA*S, *NF1*, and *KIT*. Our study recruited patients from sites in the US and Northern Europe, geographic regions in which melanoma is commonly reported. As this pilot study was designed to include a limited number of patients (up to 24), patients from other geographic regions are not represented.  |

**References**

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