Enrolment of older cancer patients in early phase clinical trials – an observational study on the experience in the north west of England
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Background
• Older patients represent the majority of cancer patients but are under-represented in early phase clinical trials (EPCTs).
• This study aimed to evaluate successful enrolment (successful delivery of the investigational medicinal product (IMP)) into EPCTs according to age (<65/65+) and identify enrolment obstacles and outcomes of patients.

Methods
• Observational retrospective study focussing on cancer patients referred to the Experimental Cancer Medicine Team (ECMT) at The Christie NHS Foundation Trust in Manchester, United Kingdom over 12-months.
• Data collected on patient demographics, co-morbidities (Adult Comorbidity Evaluation 27 (ACE-27)), polypharmacy, distance travelled and living arrangements.
• Those assessed in clinic were deemed as either suitable or unsuitable for an EPCT.
• For patients enrolled on trial, data was collected on toxicity/tolerability and treatment response
• Statistical analysis was performed at referral, new patient clinic, and during trial.
• For patients seen in clinic, the older subgroup was matched with a randomly selected cohort of younger patients based on tumour types.

Results

Patient demographics/ characteristics:
• Older cancer patients had significantly higher comorbidity score than younger patients (p <0.001) (Figure 3).

Figure 3: Distribution of comorbidities (ACE-27 score) at initial clinical assessment.
• Older patients were assessed for EPCTs at a later point in their cancer management (after at least 3 lines of treatment in 45.9% vs 28.9% for younger patients; OR 2.10; p=0.002).
• Younger patients had been enrolled in more previous clinical trials compared to older patients (15.1% vs 7.5%; OR 2.17; p = 0.05)
• Older cancer patients lived significantly closer to the EPCT unit than younger patients (p=0.045), who were travelling a median of 10 extra miles.

Suitability for EPCT
• No significant difference in suitability according to age cohorts; 16.4% for younger vs 15.1% for older cohorts (p =0.878)
• Older patients were as likely as their younger counterparts to fail pre-screening or screening procedures.
• 21% of patients assessed in clinic were successfully enrolled into EPCTs, with no difference between age cohorts (20.1% for younger vs 22.6% for older cohorts; p=0.675).

Trial outcomes
• Older patients represented 53% of the 68 patients enrolled onto EPCTs
• No statistically significant differences in outcomes between the age cohorts.
• Older patients had a proportionally lower number of serious adverse events (SAEs) (36.1% vs 53.1%; p=0.222) but a greater proportion of patients had IMP stopped due to adverse events.
• No significant differences in response rate to IMP between age cohorts
• Older cancer patients participated on EPCTs for a numerically shorter time period than younger patients (13 vs 22 weeks; p=0.330).

Discussion
• The use of 65 as an age cut off for elderly patients is a limitation
• The median age of patients referred to the ECMT was 60 years, which reflects the younger population that are referred to the ECMT compared with the general population of cancer patients.
• Older age did not affect trial enrolment or trial outcomes in this study- this is likely due to a pre-selection of patients occurring upstream prior to referral.
• Geriatric assessments/ frailty scores may help assess trial suitability in older patients.
• Designing EPCTs for older patients and engaging with primary oncologists to encourage participation of older patients in EPCTs will help trial populations become more representative of the real-world patients and help the development of the most appropriate treatments options.

Figure 1: Study flowchart.

Figure 2: Graph showing ages of patients referred and assessed for EPCTS. Of 555 patients referred to the ECMT for consideration of EPCTs in a 12-month period, the median age was 60 years. Older patients (65+ years) represented 37% (208/555) of referrals.

Figure 3: Distribution of comorbidities (ACE-27 score) at initial clinical assessment.

Referrals and access to EPCTs:

Referred for consideration of EPCTs (n=555)
- Referrals cancelled by patient or by trials team; exclusion of 84 patients

EPCTs suitability assessment in clinic (n=471)
- Age and tumour-matched random sample selection: exclusion of 153 patients (153 from younger and 20 from older cohorts)

Sample selection for EPCTs enrollment analysis (n=318)
- Younger cohort (n=159)
- Older cohort (n=158)