LACK OF CENTRALIZATION AND UNDER-RECRUITING OF YOUNG-ADULTS: LESSONS FROM EURAMOS-1/AOST0331 (NCT00134030)

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Purpose:

Investigator initiated clinical trials in rare cancers which affect children, adolescents, and young adults require multi-institutional and interdisciplinary collaboration, yet the challenges associated with such trials remain considerable. We used osteosarcoma as an example to describe the context from which patients with rare cancers are currently recruited.

Material and Methods:

Review of interim recruitment rates in EURAMOS-1, a large randomized multinational trial for patients with resectable osteosarcoma aged 0-40 years jointly performed by Children's Oncology Group (COG), Cooperative Osteosarcoma Study Group (COSS), European Osteosarcoma Intergroup (EOI) and Scandinavian Sarcoma Group (SSG) which recruited from 04/05-06/11. Analysis of institutional and age-related variables related to recruitment.

Results:

2,260 patients from 330 institutions in 21 countries* were registered (North America: 1,120 patients from 174 institutions; Europe: 1,097/147; Australasia: 42/9) (Figure 1). The mean recruitment was 1.11 patients/center/year. The degree of centralization varied considerably between countries, but an average recruitment ≥2 patients/center/year was observed for only four countries (Denmark, Netherlands, Norway, United Kingdom) (Table 1). The top 10 recruiting centers accounted for only 369/2,260 patients (16.3%), and only 3/330 participating institutions (0.1%) averaged >5 recruited patients per year. The trial was open for patients aged 0-40 years. In order to determine if all age groups participated similarly, we compared SEER incidence data [Mirabello et al. 2009] with observed age specific recruitment rates, arbitrarily defining the respective rates at age 10-14 as "1". When thus normalized according to SEER incidence data and compared to younger patients, there was moderate under-recruiting of patients aged 15-19 and considerable under-recruiting above age 19 (Figure 2).

Conclusions:

Despite attempts towards increased centralization, osteosarcoma treatment remains dispersed across multiple institutions. In this context, adolescents and particularly young adults are less likely than younger patients to be included into a "pediatric" trial, even if this is open for their age groups. A very considerable fragmentation of care needs to be taken into account when planning, performing and regulating clinical trials in rare cancers.

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Figure 1: Patients per center

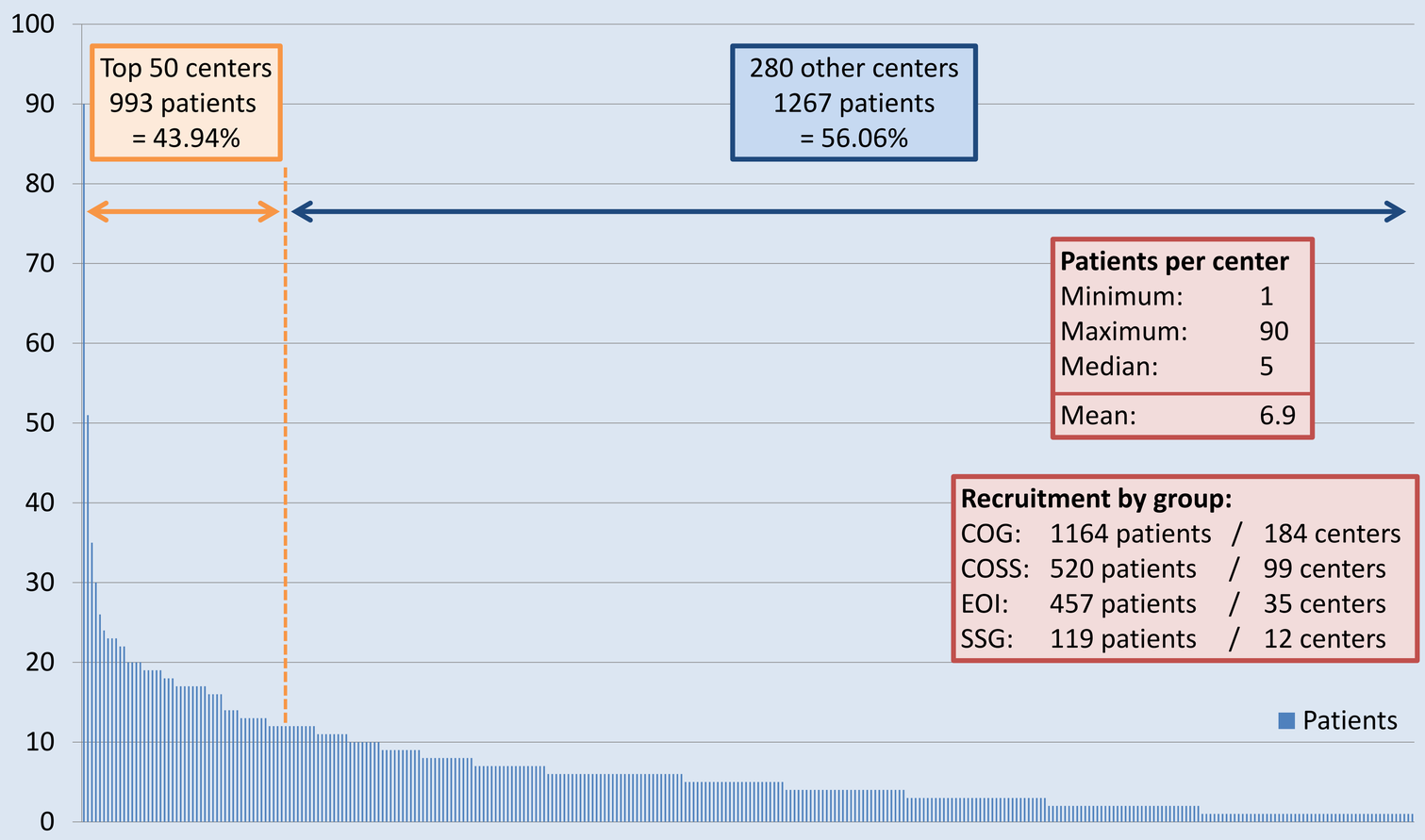

Table 1: Recruitment by country

Country	Patients		Centers		Patients / center	Patients / center / year
Australia	28	1.2%	6	1.8%	4.7	0.8
Austria	28	1.2%	5	1.5%	5.6	0.9
Belgium	52	2.3%	6	1.8%	8.7	1.4
Canada	82	3.6%	15	4.6%	5.5	0.9
Czech Republic	9	0.4%	2	0.6%	4.5	0.7
Denmark	27	1.2%	2	0.6%	13.5	2.2
Finland	3	0.1%	1	0.3%	3.0	0.5
Germany	432	19.1%	85	25.8%	5.1	0.8
Hungary	24	1,1%	2	0.6%	12.0	1.9
Ireland	6	0.3%	1	0.3%	6.0	1.0
Netherlands	101	4.5%	4	1.2%	25.3	4.1
New Zealand	14	0.6%	3	0.9%	4.7	0.8
Norway	41	1.8%	3	0.9%	13.7	2.2
Sweden	48	2.1%	6	1.8%	8.0	1.3
Switzerland	38	1.7%	8	2.4%	4.8	0.8
UK	298	13.2%	24	7.3%	12.4	2.0
USA*	1025	45.4%	153	46.4%	6.7	1.1
Total	2260	100%	330	100%	6.9	1.1

*USA incl. Puerto Rico. 4 COG centers in 3 other countries

Figure 2: Recruitment compared to osteosarcoma incidence (SEER data)