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Perspectives on Geriatric Oncology Research presented at the 2018 American Society of Clinical Oncology Annual Meeting

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1. Introduction

The 2018 American Society of Clinical Oncology (ASCO) Annual Meeting brought together oncology professionals to discuss the latest research in oncology. This year's theme: "Delivering Discoveries: Expanding the Reach of Precision Medicine" is particularly relevant for Geriatric Oncology, a field which aims at achieving personalized decision-making based on individualized risks, benefits, preferences, and values [1]. Here, we review research presented at the ASCO 2018 Annual Meeting which we consider of the highest relevance to Geriatric Oncology.

2. Geriatric Oncology Track

Since 2013, the Geriatric Oncology track has been integrated in the Patient and Survivor Care track. This year, the Geriatric Oncology track received the highest number of abstracts ever, with five selected for oral presentation (including one late-breaking abstract [LBA]), a testament to the growth of Geriatric Oncology (Fig. 1).

Although previous research has demonstrated that the geriatric assessment may predict outcomes and guide therapeutic decisions [2–5], its influence on communication and patient satisfaction had been unclear. Mohile et al. conducted a multicenter cluster-randomized controlled trial (RCT) within the University of Rochester National Cancer Institute Community Oncology Research (NCORP) to study the effects of geriatric assessment-guided interventions on communication about age-related concerns [6]. Over 540 patients aged ≥ 70 with advanced

solid tumors or lymphoma were recruited, of which 74% had ≥ 4 impaired geriatric assessment domains. Patients randomized to the geriatric assessment arm participated in more discussions about age-related concerns than controls (8 vs. 4 conversations; $p < .0001$). Additionally, these conversations were of higher quality and led to more geriatric assessment-guided interventions and higher patient satisfaction. Magnuson et al. further illustrated this in the cognitive domain, finding that discussions about cognitive concerns were higher in the geriatric assessment arm compared to controls [Odd Ratio (OR) 4.6, 95% Confidence Interval (CI): 3.0–7.2, $p < .001$], and were more notable for patients with abnormal cognitive screening (71% in the intervention arm vs. 16% in controls, $p < .001$) [7]. Findings from this study reinforce the utility and benefit of geriatric assessment in accordance with the recently published ASCO guidelines [8].

Overall survival (OS) or progression-free survival (PFS) are often the most valued outcomes in clinical trials, but this may not be the case among older patients, who may favor other outcomes such as quality of life (QoL), physical function, and cognition over survival [9]. Soto-Perez-de-Celis et al. conducted a secondary analysis of a prospective study including patients aged ≥ 65 starting chemotherapy [10]. Forty-four percent rated QoL as more important than survival, 58% either agreed/strongly agreed that they would rather live a shorter life than lose their ability to take care of themselves, and 81% agreed/strongly agreed that maintaining their thinking ability was more important than living as long as possible. In a separate abstract, Decoster et al. analyzed changes in QoL during treatment in 3673 older patients recruited to a multicenter study in Belgium [11]. They demonstrated QoL improved in 35%, and worsened in 28% of patients. Both abstracts illustrate that it is important to incorporate QoL in shared-decision making with older adults.

Several abstracts further supported the utility of geriatric assessment for predicting outcomes such as intensive care unit admission, long-term healthcare utilization, and survival [12–14]. In addition, three abstracts reported the effects of supportive care, such as pharmacy or physical activity interventions, in older patients with cancer. Ruddy et al. evaluated the feasibility of a pharmacy intervention in 60 patients aged ≥ 65 with breast, gastrointestinal, or lung cancer receiving first-line chemotherapy. The pharmacist performed medication reconciliation, obtained vaccination history, and made recommendations to the care team [15]. The intervention was feasible: 80.1% of patients approached

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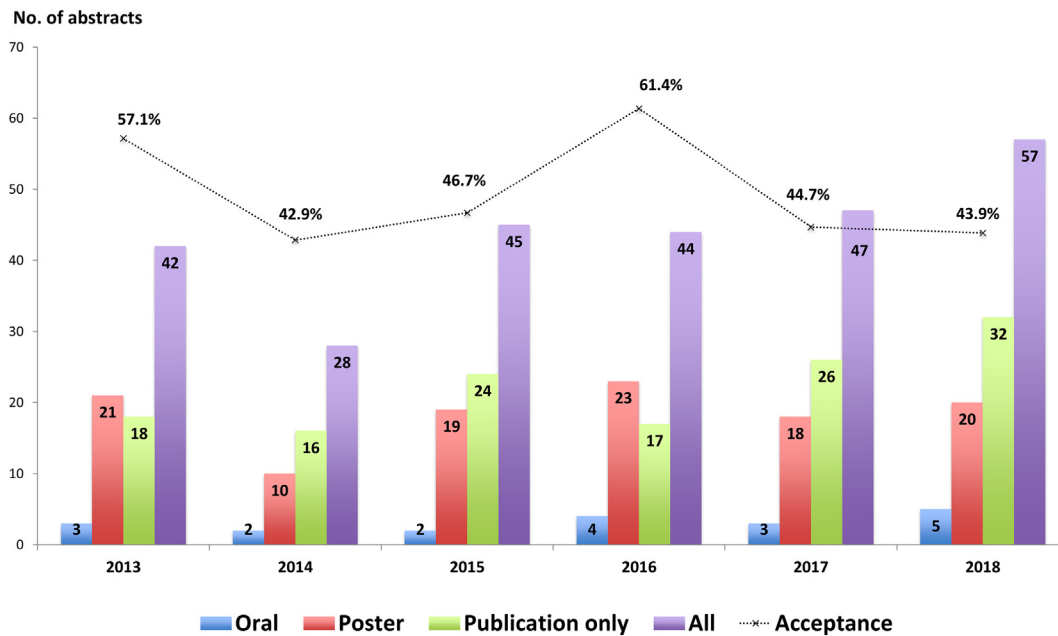


Fig. 1. Number of abstracts submitted to the Geriatric Oncology Track at the American Society of Clinical Oncology Annual Meeting and abstract acceptance rate from 2013 to 2018.

were enrolled, and 96.6% attended the pharmacist visit in the intervention arm. The intervention arm had higher vaccination rates for pneumonia (67.9% vs. 40.0%, $P = .040$) and influenza (67.9% vs. 23.3%, $P = .001$). It will be interesting to see if the benefits can be replicated in a larger study powered to detect a difference in outcomes such as inappropriate medication use, chemotherapy toxicity, and healthcare utilization. Two abstracts evaluated the effects of exercise in patients with lymphoma and carcinoma, and in patients with breast cancer receiving adjuvant radiation [16,17]. In both studies, exercise did not improve physical function and cancer-related fatigue ($P = .79$), respectively. It is unclear what the exercise adherence was in both studies, but these negative findings reinforce the need to develop exercise programs tailored to the specific needs of older patients.

3. Representation of Older Adults in Clinical Trials at the ASCO 2018 Annual Meeting

Several potentially practice-changing abstracts were presented at the ASCO 2018 Annual Meeting. We reviewed inclusion of older adults, as well as reporting of subgroup analyses of older patients, across therapeutic trials selected as LBA (Table 1).

3.1. "Less is more" in breast cancer

Three important studies focused on de-escalating therapy in women with breast cancer (BC). Sparano et al. presented the results of the TAILORx RCT assessing the benefit of chemotherapy over endocrine therapy (ET) alone in patients with localized hormone receptor-positive BC with a mid-range score [11–25] in the 21-gene BC assay [18,19]. Only 14% of patients were aged ≥ 65 ($n = 950$), and those aged ≥ 75 were excluded. The study protocol states that this population was excluded because their limited life expectancy would make ten year follow-up very difficult [18]. The proportion of patients with low, mid-range, and high scores was not different between patients aged ≥ 60 and their younger counterparts [18]. Overall trial results showed that adjuvant ET and chemotherapy plus ET had similar efficacy, and these results were mirrored among the older women included.

The PERSEPHONE study, although not selected as a LBA, may be of particular relevance for older patients with HER2-positive BC [20]. In

this non-inferiority RCT, 4088 women with HER2-positive localized BC were randomized to twelve vs. six months of adjuvant trastuzumab. PERSEPHONE showed that six months of trastuzumab was non-inferior to twelve months, with a 50% reduction in clinically significant cardiotoxicity. However, age-specific analyses were not included, and we eagerly await the report of outcomes and adverse events among older participants.

The Japanese RESPECT non-inferiority RCT by Sawaki et al. assigned 266 patients aged ≥ 70 with stage I-III HER2-positive BC to adjuvant chemotherapy plus trastuzumab for twelve months or to trastuzumab alone [21]. Patients with hormone receptor-positive BC additionally received ET. Patients receiving trastuzumab alone had significantly less adverse events and less deterioration in QoL at six months. However, non-inferiority of trastuzumab monotherapy could not be demonstrated, mainly because of the small number of DFS events (only 30 patients had recurred at three years in both arms). However, a supplemental analysis of restricted mean survival time showed that the lost survival due to omitting chemotherapy was less than one month at three years. Although results from this trial will not lead to practice changes, they are certainly provocative and should be explored further.

3.2. Prolonging Survival in Pancreatic Cancer

An important advance in the field of gastrointestinal oncology was the PRODIGE 24/CCTG PA.6 RCT by Conroy et al., which allocated patients with pancreatic cancer after pancreatectomy to adjuvant chemotherapy with gemcitabine or mFOLFIRINOX (oxaliplatin, irinotecan, and 5-fluorouracil) [22]. mFOLFIRINOX significantly improved OS compared with gemcitabine (54.4 vs. 34.8 months; HR 0.59, 95% CI 0.46–0.76). Patients aged ≥ 80 were excluded, and median age was 64 (range 30 to 81). In subgroup analyses, the benefit of mFOLFIRINOX was unclear among patients aged ≥ 70 [HR for disease-free survival (DFS) 0.86, 95% CI 0.53–1.39]. It will be relevant to see if this is due to increased toxicity or treatment interruptions among older patients.

3.3. Novel Therapies for Soft Tissue Sarcoma in Older Adults

Older adult-specific phase II clinical trials are of paramount importance, and ASCO has recommended conducting them in order to

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