Selected presentations

Featured papers from the past year

Smartphone monitors chemotherapy toxicity

Among papers highlighted in the opening plenary was one showing that a 15% decline in daily number of steps -- identified by a pedometer app installed on a smartphone -- gives a clear signal of chemotherapy toxicity. Data derive from a pilot study in forty elderly patients from Mexico. All but three patients used the smartphone appropriately.

Sixty percent had their toxicities managed over the phone, while 28% were sent for urgent medical attention. This technology holds promise, especially where healthcare resources are limited, Enrique Soto Perez De Celis et al conclude in *J Geriatr Oncol 2018;9:145-151.*

Bend or break?

In relation to risk and resilience in adjuvant breast cancer, a secondary analysis of the randomized CALGB 49907 trial shows that 42% of participants aged 65 and older reported a decline in physical function over the course of chemotherapy. But half of these women said they had recovered by twelve months.

Risk factors for having lower twelve-month function included dyspnoea and being unmarried. Pre-treatment fatigue predicted decline in physical function during chemotherapy, reported Arti Hurria et al in *J Am Geriatrics Soc August 2018.*

Pre-op cognition, mobility, function

To optimize care of older patients, the American College of Surgeons NSQIP Geriatric Surgery Pilot suggests data on pre-operative cognition, decision making, mobility and function should be included when modeling overall surgical and geriatric-specific outcomes such as postoperative delirium, new mobility aid use, functional decline, and pressure ulcers. *Berian JR et al, J Am Coll Surg December 2017.*

Palliative and supportive care: same or different?

In the old model, potentially curative treatment changes abruptly to palliative care if the aim of cure is not achieved. In contrast, the current concept is one in which disease-modifying or potentially curative treatment is accompanied throughout its course by supportive/palliative treatment. The latter increases as the intensity of disease-modifying treatment is reduced in patients who are approaching death.

The concept of early palliative care designed to manage distressing clinical complications (an approach acknowledged by the WHO) has led to a number of studies including PALCOM in Barcelona (*Tuca A et al, Support Care Cancer 2018*). This identified high symptom burden, difficult pain and reduced functional status as factors that predicted problems that were complex and difficult to manage in advanced cancer.

At the supportive care session held jointly with MASCC, Andrew Davies (St Luke's Cancer Centre, Guildford, UK) described how the recent Cochrane Review supports the idea that palliative care begun at the time advanced cancer is diagnosed can reduce morbidity, increase quality of life and decrease carer burden. https://www.cochrane.org/CD011129/SYMPT_early-palliative-care-adults-advanced-cancer But the idea that it improves survival may be less well-founded: the benefit seen in the 2010 Temel et al study of early palliation in metastatic NSCLC has not been replicated, Dr Davies noted.

He ended by sharing the encapsulation – uncertain in provenance but certain in relevance: *To cure sometimes, to relieve often, to comfort always. This is our work.*

Frailty in haematological cancers

Functional status predicts transplant outcomes

The value of IADL as a predictor of outcomes in allogeneic haematopoietic stem cell transplantation is supported by new data from the University of California San Francisco, USA, presented by Li-Wen Huang. Having one or more IADL impairment was associated with poorer OS: median 16 months vs not reached in patients with no IADL deficit. For progression-free survival, the corresponding figures were a median of 8 months in the presence of an IADL deficit and 43 months in patients with no deficits. On univariate analysis, age, comorbidities, disease risk and intensity of transplant chemotherapy were *not* associated with PFS, OS, or grade 3 and greater AEs. The MOS Physical Health Score was related to poorer OS and alloHCT toxicity, being predictive of non-relapse mortality, grade 3 and greater AEs, and length of hospital stay. Li-Wen Huang concluded that cancer-specific geriatric assessment measures in general -- and IADL in particular -- could usefully be incorporated into pre-transplant risk assessment for older adults deemed fit for HCT. The single-institution study involved 148 patients with a median age of 62 years. The majority had AML or MDS. Interestingly, although both AML and MDS are diseases of older adults, only 3% of patients aged sixty or older receive alloHCT. In younger patients, the figure is 28%.

New frailty index in multiple myeloma

Combining age, comorbidities and WHO PS (as a proxy for ADL and IADL) gives a frailty score which is predictive of overall survival in elderly patients with newly diagnosed multiple myeloma, according to data from the HOVON/Nordic Myeloma Study Group presented by Claudia Stege of the Free University of Amsterdam Medical Centre, the Netherlands. Frailty was clearly associated with poor OS: median 74 months in fit patients, 56 months in the unfit, and 45 months in the frail. But frailty did not relate significantly to PFS, where the corresponding figures were a median of 25, 19 and 21 months respectively. Risk of grade 3 or greater infection was highest in the frail group, intermediate in the unfit, and lowest in the fit group. Better fitness was also associated with overall risk of AEs, but not with haematological AEs.

Treatment differences only sometimes affect survival

Do different treatment strategies affect outcome in older women with non-metastatic breast cancer?

When it comes to endocrine therapy, variations between countries seem not be important for outcome. But in locally advanced breast cancer, countries with high levels of surgery have better survival rates. So data coming from the EURECCA Breast Cancer Project present a somewhat complicated picture, Johanna Portielje (University of Leiden, the Netherlands) told the Amsterdam meeting. Data on more than a quarter of a million breast cancer patients aged seventy or over were collected from registries in the Netherlands, Belgium, Ireland, England and Poland. The proportions of patients receiving various forms of local and systemic treatments were compared against five-year relative survival. Even adjacent countries showed surprisingly large differences in treatment strategy: while 85% of women with stage 1 breast cancer had endocrine therapy in the Netherlands, this was true of only 20% of women in Belgium. Yet survival outcome was very similar. In Belgium, only 22% of stage III patients did not have breast surgery, while this figure was 51% in Ireland. In this instance, Ireland did have significantly worse relative survival, suggesting undertreatment. Where the comparative data suggest that different treatments impact outcome, hypotheses generated should be tested in randomised trials.

Pragmatic “plan of the day” approach to bladder RT

Adapting the radiotherapy plan to the state of the bladder *at the time of treatment* can improve accuracy and tolerability in patients with muscle invasive disease who are unsuited to radical therapy, reported Shaista Hafeez (Royal Marsden Hospital, Sutton, Surrey, UK). Such precisely adapted planning can reduce by half the volume of healthy tissue irradiated, she estimated, allowing good local control to be achieved with acceptable acute and delayed toxicity. In a phase 2 study, 55 patients (median age 86 years) who were ineligible for cystectomy or daily radiation received six, weekly, image-guided hypofractionated treatments to a total of 36 Gy. The overall plan was to treat the whole, empty bladder.

But bladder shape and volume vary as it fills and according to pressure from adjacent organs, notably the rectum. So it helps to have a *library* of plans from which to choose on the day of treatment. In forty percent of sessions included in the study, treatment was adjusted to increase or reduce the margin treated. OS at one year was 60%.

Sarcopenia speeds up at time of cancer diagnosis

The point of cancer diagnosis in older adults is associated with an acceleration in the rate at which lean muscle mass declines. This change is most evident in people with lung and prostate tumours. At comparable age, adults who are not diagnosed as having cancer do not show the same increased rate of muscle loss.

These findings -- from the Health, Aging and Body Composition (Health ABC) study -- were presented by Grant Williams, of the University of Alabama School of Medicine, Birmingham, USA. In the longitudinal study, data were collected for six years on 3075 initially healthy 70-79 year olds who enrolled in 1997-1998. During follow-up, 515 patients developed cancer.

Before diagnosis, lean body mass was falling at a faster rate in those who would go on to develop cancer than in those who would not – but from a higher baseline (mean 49 vs 46kg). At the time cancer was diagnosed, those affected had a lean mass roughly the same as those who did not have a cancer diagnosis. From that time onwards, the rate of muscle mass decline in those with cancer became markedly steeper while the slope in those without cancer remained the same.

Muscle loss data were adjusted for age at enrollment, sex, gender and ethnicity.

Sarcopenia is an important phenomenon since it is associated with increased rates of chemotherapy toxicity, surgical complications and poorer survival – as in colorectal cancer (*Caan BJ et al. Cancer Epidemiology, Biomarkers and Prevention 2017*).

Patient-computer interaction predicts better survival

The ability to complete a pre-operative electronic rapid fitness assessment (eRFA) *without help* relates to lower mortality at one year in older patients having surgery, Armin Shahrokni (MSKCC, New York) told the Amsterdam meeting. The prospective study involved 800 patients aged 75 years and over who had a postoperative stay in hospital of at least a day. One year mortality among the 389 patients who completed the pre-op assessment without help was 15.7%, but it was 22.7% in those who had help or let someone else do the eRFA for them. The age of those who completed the assessment independently was little different from the age of those who could not (79 vs 81 years). Mean time to completions was ten minutes. Inability or unwillingness to interact with the tablet to complete the eRFA seems in itself to be an indication of relative frailty.

Radiosurgery an option for brain mets in over 65s

Gamma knife radiosurgery (GKRS) for brain metastases is a reasonable treatment option in patients aged 65 years and older: survival benefit and toxicity profile are similar to that experienced by younger patients, Isaaco Desideri (Careggi Hospital, Florence, Italy) reported. Interestingly, the G8 is not a helpful screening tool in this elderly population.

Restrospective data come from a series of 89 patients who had GKRS during the period 2012-2017 to treat up to 14 brain mets. Median OS was 14.2 months in patients aged 65-74 years and 15.7 in those aged 75 and over. Median PFS was 8.3 months and 7.8 months in the two groups.

The OS curve for patients with a G8 score less than 14 largely overlapped that for patients with higher scores. The number of treated mets was not a prognostic factor.

Optimise concomitant drug use in ovarian cancer CT

Being able to complete chemotherapy improves survival in women with ovarian cancer. Aspects of polypharmacy may stand in the way.

Giving the results of a study from Denmark, Trine Jorgensen (Odense University Hospital) described how older ovarian cancer patients taking a mix of drugs that put them at risk of two or more potentially adverse interactions were more than twice as likely as others to end chemotherapy before completion of the course.

Those taking three or more potentially inappropriate medications had twice the mortality rate of those who were not taking any such medications (median OS 22 vs 48 months).

But polypharmacy per se was not independently associated with completion of chemotherapy or with mortality.

Analyses were adjusted for FIGO stage, surgical regimen and outcome and other potentially interacting variables. The Danish register contains data on almost four thousand women diagnosed with epithelial ovarian cancer in the period 2005-14 who had chemotherapy. The study focused on those aged 70 years and older.

Different pattern of toxicity with immunotherapy in elderly

While anti-PD(L)1 therapies are a valuable option in older patients, they should be closely monitored for significant immune-related toxicities since age seems to increase risk, Capucine Baldini (Gustave Roussy, Villejuif, France) told an oral abstract session.

Over the period June 2014 to October 2017, 615 patients treated with anti-PD(L)1 antibodies were prospectively included in the Registry of Severe Adverse Reactions to Immunomodulatory Antibodies

used in Oncology (REISAMIC), initiated by the Institut Gustave Roussy. 191 patients were aged seventy or older. Data were collected on the incidence and management of grade 2 or greater immune-related AEs.

Compared with their younger counterparts, older patients were more likely to have melanoma, and less likely to have NSCLC. They were more likely to receive pembrolizumab and less likely to be treated with nivolumab.

In comparison with younger patients, those 70 years and older were substantially more likely to experience skin toxicity (50% vs less than 30%) and more likely to have liver toxicities (10% vs less than 5%). On the other hand, they were less likely to experience endocrine toxicity (15% vs 25%) and GI toxicity (8% vs 16%).

Corticosteroids were used for a similar length of time to treat immune-related toxicities in older and younger patients (124 and 131 days). Median time to emergence of toxicity was ten weeks in younger patients and six weeks in those who were older. Of older patients, 14% stopped treatment because of toxicity. This compared with 7% in younger patients.

Complex barriers to trial accrual

Older patients are just as likely as younger patients to accept enrollment into a trial if one is offered. But – despite the efforts of SIOG and others -- the numbers actually accrued remain disappointingly low. This seems to be due to a range of physician-related factors, which differ in interesting ways between academic and community-based oncologists.

Based on 44 qualitative, semi-structured interviews carried out in 2018 by Mina Sedrak and colleagues from City of Hope, Duarte, California, it seems that community oncologists perceive patient attitudes and beliefs and caregiver burden as important obstacles to trial entry. Academics saw poor accrual as arising more from physician factors, notably bias and the need for physician time and support. Strict eligibility criteria for trial entry and concerns about potential toxicity were perceptions shared by community and academic oncologists.

Time to close the mortality gap in APL

Acute promyelocytic leukaemia accounts for around 10% of acute myeloid leukaemias and, unlike other forms of the disease, does not increase in frequency with age. When it does occur, APL has the feature of being highly treatable using well-tolerated regimens. And this is true to the extent that the question of establishing whether an older person is fit for therapy really no longer applies. We owe this success to the differentiating agent all-trans retinoic acid (ATRA) and arsenic trioxide (ATO), which allow targeting of the PML/RARa fusion protein that underlies the disease.

Ramy Rahmé (Hôpital Saint Louis, Université Paris Diderot, France) and colleagues reported this year in *Haematologica* the results of their APL 2006 trial in which123 standard-risk patients older than 70 years were treated with ATO plus ATRA and a reduced-dose anthracycline. CR was achieved in 92% of cases, and the five year OS was 80%.

At the moment, the overall five year survival rate in older APL patients falls well below this figure, and is also well behind that of younger patients: data from the Netherlands suggest survival in APL patients aged 41-60 years is 75% while in patients older than 70 it is 37%. Such discrepancies require us to actively encourage the early diagnosis, prompt referral, and definitive treatment of elderly APL patients, Heidi Klepin (Wake Forest School of Medicine, Winston-Salem, North Carolina, USA), who co-chairs the SIOG APL Task Force, told the Amsterdam meeting. Task Force recommendations should be published in 2019. Of course there are challenges. One is treatment cost; another is the non-availability of ATO in many countries. The usual suspects -- comorbidity and polypharmacy, particularly the risk of drug interactions that may cause QT prolongation – also contribute to the complexity of treating older patients with APL.