a platinum in some centers, based on UK trials. Therefore several options can be proposed as reference regimens: the doublets of a fluoropyrimidine (5-FU or capecitabine) plus cisplatin (or oxaliplatin) or triplets of DCF or ECF (or ECC or EOC). The median survival is however usually still in the range of 8−11 months in most modern trials. Recently, the benefit of second line chemotherapy has been also demonstrated with a modest, but clear impact of a second line regimen (irinotecan) compared to BSC.
Although gastric cancer is relatively chemosensitive (RR 30−40%), the outcome remains poor. The complete response rate is extremely low and the response duration is short. Moreover the combinations regimens are relatively 'heavy' for patients often in poor general condition. There is therefore a clear need for better treatment options. The research on targeted agents has been intensified recently. The doublet of 5FU/capecitabine and cisplatin serves often as a backbone for the combination with novel targeted agents. A significantly longer survival has been shown for the combination of a fluoropyrimidine/cisplatin plus trastuzumab in patients with a HER-2 positive gastric or gastro-esophageal junction adenocarcinoma compared to the cytotoxic doublet alone. Several other targeted agents are under investigation in combination with cytotoxics (angiogenesis inhibitors, epidermal growth factor inhibitors or other anti-HER2 inhibitors) or also as monotherapy (mTOR inhibitor everolimus) and offer the hope for an improved outcome.

305 INVITED

Integration of targeted therapies

J. Tabernero[1], F.J. Ramos[1]. [1]*Vall d'Hebron University Hospital, Medical Oncology Department, Barcelona, Spain*

Gastric cancer (GC) is the second leading cause of cancer mortality in the world. Advanced GC patients have a poor prognosis. Palliative chemotherapy improves survival, as compared with best supportive care. Although oxaliplatin, docetaxel and capecitabine have demonstrated activity in recent phase III trials the median overall survival (mOS) remains poor [1−2], therefore novel treatment options are urgently needed. New biological therapies aim to inhibit different targets of signal transduction pathways that are thought to be functionally selective or overexpressed in certain tumor types. GC belongs to these tumor models with overexpressed signal transduction pathways that are potential targets of a number of new drugs that are currently being in clinical development (see Table).
Recognition of the vascular endothelial growth factor (VEGF) pathway as a key regulator of angiogenesis has led to the development of several VEGF-targeting agents. At present, available clinical data on the use of angiogenesis inhibitors are limited to nonrandomized phase II trials. The combination of bevacizumab and chemotherapy showed encouraging efficacy results: response rate (RR) ~65%, median time to progression (mTTP) ~8 months and mOS greater than 12 months [3−4]. However, the favorable efficacy results were counterbalanced by bevacizumab-related toxicities: gastric perforation, thromboembolic events and hemorrhage. An ongoing international phase III trial (AVAGAST) will elucidate the role of bevacizumab in the first-line setting. Sunitinib and sorafenib, two multi-tyrosine kinase inhibitors (TKIs), are being tested in the first- and second-line setting with promising preliminary results.
The epidermal growth factor receptor (EGFR) is a tyrosine kinase receptor that belongs to the ErbB family. EGFR is highly expressed in patients with advanced GC. Several phase II studies combining cetuximab with either irinotecan/5-fluorouracil(5-FU)- or oxaliplatin/5-FU-based chemotherapy have demonstrated encouraging activity: RR $\approx$ 50−65%, and mOS of 9.5−11.7 months [5−6]. Unfortunately, all these trials are limited by their nonrandomized design. An ongoing international phase III trial (EXPAND) will define the role of cetuximab in combination with capecitabine and cisplatin in the first-line setting. EGFR inhibitors are also being evaluated as second-line treatment in advanced GC. The human epidermal growth factor receptor 2 (HER2) is overexpressed in ~22% of GC patients. In an international phase III trial of patients with AGC the addition of trastuzumab to standard first-line chemotherapy showed a statistically significant improvement in the mOS of patients with HER2-positive GC. Trastuzumab in combination with chemotherapy (5-FU or capecitabine and cisplatin) has become a new standard option for the first-line treatment of HER2-positive GC patients.
Other potential targets, including other receptors (c-Met, IGF-1R), proteins involved in cell cycle regulation, proteasome, matrix metalloproteinases, histone deacetylases and chaperone proteins, have been demonstrated to be critical in the balance of the tightly regulated pathways that promote either cell survival or cell death. New drugs are being developed against those specific targets and preliminary clinical and clinical evaluation of these compounds is expected in the near future.

References

[1] Van Cutsem E *et al*. *J Clin Oncol* 2006;24:4991–4997.
[2] Cunningham D et al. *N Engl J Med* 2008;358:36−46.
[3] Shah MA et al. *J Clin Oncol* 2006;24:5201–5206.
[4] Jhawer M et al. *Proc ASCO GI Cancer Symposium 2009*.
[5] Pinto C *et al*. *Ann Oncol* 2007;18:510–517.
[6] Han SW *et al*. *Br J Cancer*. 2009;100:298–304.
[7] Van Cutsem E *et al*. *J Clin Oncol* 2009;27(18S):LBA4509.

Scientific Symposium (Thu, 24 Sep, 09:00−11:00) **Fertility and sexuality: the development of oncosexology**

306 INVITED

Fertility: Understanding the options after cancer treatment

L. Schover[1]. [1]*UT M.D. Anderson Cancer Center, Department of Behavioural Science, Houston, USA*

Because most people with cancer are over age 50, fertility is mainly a concern for those diagnosed in childhood, adolescence, or young adulthood. It is interesting to compare the explosion of interest and research funding focused on fertility preservation, compared to the relatively small increase in attention to assessing or treating sexual dysfunction in men and women with cancer–problems that affect at least 50% of survivors, are profound, and do not improve over time without intervention.
However, cancer-related infertility also can cause profound emotional distress that does not disappear with time. In a recent survey of over 250 women diagnosed at age 40 or less, those who desired a child at the time of cancer diagnosis and were unable to have one were significantly more distressed at a mean of 10 years after cancer treatment than women whose childbearing was not interrupted. Smaller studies of men also have suggested long-term grief over infertility after cancer.
Fortunately, sperm banking is a practical option for 90% of men diagnosed with cancer. Although the choices for women are more expensive and less reliable, recent advances in vitrification of oocytes, use of immature oocytes matured in the laboratory, and banking/autotransplantation of ovarian tissue are gradually approaching the efficacy of ovarian stimulation with cryopreservation of embryos. Some cancer treatments have also been modified to spare fertility, for example less toxic chemotherapy for Hodgkin disease, ovarian transposition before pelvic irradiation, or conservative surgeries like trachelectomy or removal of only one ovary for low-stage ovarian cancer.
A major problem is that choices about preserving fertility must be made at the time of maximum stress, when a cancer diagnosis is recent and treatment planning is underway. It is difficult for younger patients to understand their disease and treatment plan, let alone to take the time to weigh the costs and benefits of options to store gametes or embryos for the future. Parents may also have to make decisions for their very young children that involve an additional minor surgery to collect tissue. Most settings do not have counselors with time to teach patients about their options much less to help them sort out their emotions.
After cancer treatment, some men and women will remain fertile or will recover fertility. They often have intense anxiety about whether their offspring will have special risks for cancer or will have a greater chance of a birth defect related to the parent's cancer treatment. Those relatively few who carry a mutation involved in a hereditary cancer syndrome now have the option of using prenatal diagnosis or preimplantation genetic diagnosis to avoid passing on their damaged gene. For women, another worry is whether pregnancy could provoke a cancer recurrence. Women are less aware of risks that subclinical cardiac or pulmonary impairment could become life-threatening during the stress of a pregnancy.
For those who remain infertile, adoption is not easy. International adoption countries may exclude cancer survivors, make them wait 5 years out, or want a letter from the oncologist. Domestic agencies and birth mothers also may be loathe to give a child to a couple when one spouse has had cancer. Adoption is also quite expensive in most Western countries. Third-party reproduction includes use of donated sperm, oocytes, or embryos, and/or a gestational carrier. Only a minority of cancer survivors are willing to consider these paths to parenthood.

307 INVITED

Talking about sex: identifying psycho-sexual concerns in the clinic

I. White[1], D. Kelly[2]. [1]*University of Surrey, Division of Health and Social Care, Guildford Surrey, United Kingdom;* [2]*Middlesex University, School of Health & Social Sciences, London, United Kingdom*

Background: Multi-modal cancer therapy has led to significant improvements in disease control and survival. However this comes at a price in