binds to membrane receptors (types I and II serine/threonine kinases) that signal via the Smad pathway. Smads are signalling molecules, acting as transcription factors for genes coding for procollagens and other matrix compounds, and fibrogenic growth factors. Alternative signalling routes from the TGFb1 receptor (TGFb1R) complex to the nucleus bypass cytoplasmic Smad proteins, using the so-called p38, JNK, ras/ERK MAP kinase and Rho/rho kinase (ROCK) pathways. Anti-TGF-b1 strategies including soluble RII have shown efficacy to prevent and halt radiation-induced fibrogenic process and recently Pirfenidone has shown some effectiveness in halting diabetic nephropathy and IPF in humans. No trial is scheduled on radiation fibrosis, however due to the pleiotropic role of TGF-b1 in tissue homeostasis serious side-effects can be anticipated.
TGFb1 is not the only fibrogenic cytokine, the products of Thy-2 lymphocytes can be mentioned including IL-4 and IL-13. Amongst the growth factors bFGF, PDGF, IGF; and several chemokines such as ET-1 and CTGF form a longer list of potent fibrogenic factors acting alone or in conjunction with TGFb1.
PDGF family mainly target mesenchymal cells. Their physiological and fibrogenic actions are achieved by homodimerisation of the growth factors (creating PDGF-AA, PDGF-BB etc dimers) that bind to specific plasma membrane receptors (PDGFR-a and PDGFR-betc). PDGFR-a is transactivated by TGF-b1 and is especially associated with fibrosis. PDGF signals through major transduction pathways including PI3K, Ras/MAPK and PLCg to stimulate myofibroblast proliferation and extracellular matrix synthesis. Targeting PDGF pathway using Glivec prevented radiation-induced pulmonary fibrogenesis. Clinical trials are ongoing in systemic sclerosis, nephropathy and IPF but no specific trial on radiation fibrosis is planed so far.
CTGF is a matricellular protein that promotes fibroblast proliferation and ECM production *via* a yet uncharacterized membrane receptor. CTGF inhibition using anti-CTGF monoclonal antibody and Pravastatin has shown very promising results in both preventing and reversing radiation fibrosis in experimental rodent model. Therefore the anti-fibrotic efficacy of Pravastatin is currently investigated in a phase II/III study at IGR.

Special Session (Sun, 25 Sep, 13:15−14:15)
Fertility Concerns

150 INVITED

Frozen Hope − Fertility Preservation for Women With Cancer

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Increasingly successful treatments for cancer and higher survival rates mean that considering future fertility is an important factor in the treatment of pre menopausal and nulliparous women and younger girls. The parallel scientific and clinical advances in reproductive technologies now present more options for the preservation of fertility at the time of treatment for cancer and assisted conception may be used for reduced fertility later in life.
The diagnosis of any type of cancer is usually devastating and confronting mortality and the other complex emotional, social and practical issues associated with preserving fertility is not easy for patients or practitioners when dealing simultaneously with all the other decisions.
Understandably the immediate emphasis is on the treatment for cancer and it may be difficult to think beyond to life later on. The psychological impact of the prospect of infertility may be mitigated by freezing embryos or oocytes (eggs). For women, the options for preserving their fertility depend on individual medical and social circumstances. Embryo freezing, first successful in 1983, is now a routine part of in vitro fertilisation cycles (IVF) but can only be used if the woman has a partner to create embryos or uses donated sperm. Cryopreservation of oocytes may be preferred by many women but it has proved more technically challenging. Although the first live birth from a cryopreserved oocyte was reported in 1986 the success rates remain low and it is much less widely available than embryo freezing. Research is ongoing into freezing ovarian tissue and this may be an option in the future. Most people would choose to have their own genetic children but using donated eggs may be considered by women who are infertile after the treatment for cancer if preservation of embryos or oocytes fails or are not chosen for medical or personal reasons. The window of opportunity for preserving embryos and oocytes is limited and a decision may have to be made about whether to delay starting treatment to take advantage of these options. However with the advances in fertility preservation and treatment, an integral part of cancer care should be discussing the implications for reproduction and counselling patients to help with their decisions. The legal and regulatory framework will also impact on what may be offered, for example embryo freezing is not allowed in some countries. Some cancer centres have established links with assisted conception units to provide fertility oncology services but this is not yet routine.

151 INVITED

Male Infertility and Cancer

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Many cancer treatments increase the risk male infertility, particularly those involving irradiation of the pelvis and/or systemic treatment with chemotherapy drugs. Hence, the opportunity to bank sperm, before cancer treatment begins, is invaluable for many males as 'fertility insurance'.
Sperm banking has been technically possible since the 1950's, but the organisation of sperm banking services as part of oncology care only became developed in the 1970's. In spite of this long history, their remains considerable evidence today that many males are often not given the opportunity to bank sperm (or when it is offered they do not accept it). Consequently, the ability of some men to father children post-treatment will be compromised if their fertility does not recover.
The prospects of sperm production recommencing following cancer treatment among men who bank sperm is quite good with only a third of men remaining azoospermic in the long-term. However, data on the probability of male cancer survivors achieving paternity spontaneously (i.e. without assisted conception) is less clear with some studies providing conflicting estimates of how likely fatherhood may be.
If necessary, frozen-thawed sperm, or freshly ejaculated sperm (if some natural fertility returns), may be used in a variety of assisted conception procedures including Intra-Cytoplasmic Sperm Injection (ICSI). Even in men who are azoospermic after cancer treatment, current data suggests that sufficient numbers of sperm can sometimes be obtained from testicular biopsy to make fertilisation of oocytes using ICSI possible.
The long-term health outcome of children born to cancer-survivors is thought to be very good, although there are few studies that have looked at this cohort specifically. However, singleton babies born through assisted conception (using frozen or fresh sperm) are healthy as their naturally conceived counterparts. There is increasing recognition that the major adverse outcomes are associated with multiple births.
Unfortunately, for pre-pubertal males who could not bank sperm, or in post-pubertal males who were too ill or where banking was not offered, there are no known therapies to stimulate sperm production if it does not return naturally at the end of treatment. In such cases, the use of donor sperm or adoption remains the only known methods to allow such men to establish families.

152 INVITED

Same Sex Couples Fertility Issues

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I have made a Pub Med database search to see if there are differences concerning fertility issues between same sex couples and heterosexual couples.
The review did not find any publications concerning same sex couples fertility issues.
There are no differences in how to preserve fertility in heterosexual- or same sex couples.
The differences concern the attention on homosexual realities and psychosocial needs.
It has been shown that providers not inquire about sexual orientation. Same sex couples were afraid to reveal their sexual orientation out of fear of stigmatization and homophobia.
It is of great importance that the ambiance in healthcare is open concerning sexual orientation and that health givers ask about sexual orientation to make same sex couples feel at ease and then dare to disclose their sexual orientation.

Special Session (Sun, 25 Sep, 13:15−14:15)
Esophageal Cancer − Ways to Improve Outcome

153 INVITED

How Radical Should Surgery Be?

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Esophagectomy for carcinoma can be viewed as being comprised of two components: resection of the esophagus and resection of the enveloping lymphatics. Controversy exists regarding how radical, or extensive these two components should be. Non-radical (standard) resection of the esophagus involves simple extirpation of the organ,