2005 were managed with emerging ablative techniques, in contrast to 22%, 17%, 33% and 18% having laparoscopic partial nephrectomy, open partial nephrectomy, laparoscopic or open radical nephrectomy, respectively.

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36 INVITED

Novel targeted and signalling pathway inhibitors: an overview

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Abstract not received.

37 INVITED

Novel targeted and signalling pathway inhibitors – ongoing studies

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Global investigators have combined their efforts in groundbreaking landmark trials which have changed our perception of metastatic RCC.
AVOREN study: AVOREN is an international European phase III double blind randomized placebo control trial which included 649 pts with advanced clear cell carcinoma in >50% of the specimen after nephrectomy. Pts were randomized between IFNα and placebo and the combination of Bevacizumab and IFNα. Although OS survival was to have been the primary endpoint, the trial was stopped by the IDMC after an improvement in PFS was seen and pts were offered Bevacizumab. A similar study is ongoing in the US cooperative groups.
PAZOPANIB Trial: Pazopanib is a potent, multi-target receptor TKI of VEGFR-1, -2, -3, PDGFR-a and -b and c-kit. A Phase III randomized global study has compared Pazopanib to matching placebo, in a 2:1 ratio, in pts with locally advanced or metastatic RCC. Of 435 pts entered, approximately 1/2 had prior cytokines and 1/2 had no prior therapy. The 1º objective is to evaluate PFS. The 2º objectives are OS, objective RR, adverse events and QOL.
RECORD-1 Trial: RAD 001 (Everolimus) is an oral mTOR pathway inhibitor, an active Rapamycin derivative, not a prodrug. Renal Cell Cancer Oral RAD 001 given Daily (RECORD-1) is a multicenter international phase III trial in 362 pts with progressive metastatic disease. RAD 001 plus BSC compared to BSC and placebo in pts who have progressed after antiogenesis TKIs (Sunitinb and Sorafenib). PFS is the primary objective. Secondary objectives include: OS, response and duration, safety, disease related symptoms and QOL. Exploratory evaluation of serum and tissue biomarkers will be evaluated.
BEST Trial: The BEST ECOG trial is designed for 360 pts with untreated advanced RCC and will randomize pts to 1 of 4 treatment arms: Bevacizumab, Bevacizumab plus Temsirolimus, Bevacizumab plus Sorafenib and Sorafenib plus Temsirolimus. This trial may be criticized for not including a Sunitinb arm, which is at the moment considered to be a new standard of therapy in the 1st line setting.
AMGEN trial: Angiopoietin-2 (Ang-2) is a regulator of angiogenesis. An inhibitor (AMG386) to Ang-2 is being evaluated. Because this represents an alternative pathway to VEGF-mediated angiogenesis, the potential exists for combining inhibitors of this pathway with current anti-VEGF approaches.
EFFECT trial: This phase III will evaluate the combination of Sunitinib plus IFNα. The planned multicenter phase III study will evaluate 3 treatments. Sunitinib, 50 mg/day orally, 4 weeks on 2 weeks off (the intermittent, FDA-approved dosing), Intermittent Sunitinib plus IFNα and Sunitinib continuous dosing. Planned accrual is 499 pts.
TROVAX Trial: TroVax delivers a novel tumor associated antigen (5T4) using Modified Vaccinia Ankara vector An international, randomized, double blind study to investigate whether TroVax, added to 1st-line standard of care, prolongs survival: sc IL-2, sc IFNα or Sunitinib. The 1º endpoint is OS. 700 pts will be enlisted.
Many trials of novel combinations are underway, vertical combination therapy targeting the same pathway (i.e. Sorafenib and Bevacizumab), horizontal targeting of different pathways (i.e. Sunitinb and Erlotinib) and other combinations which target distinct mechanisms of action (i.e. high-dose IL-2 plus Bevacizumab or IFN + Sunitinib).
It is extremely likely that combinations of agents will emerge as important approaches to treatment. Since direct comparisons of these agents have not yet been made, they have all emerged as promising and viable options. It is unknown to what degree these agents are cross-resistant and whether combination therapies or sequential therapy with cytokines or with Bevacizumab or with TKI will improve prognosis. It will be important to evaluate how these therapies work through analysis of patients with both responsive and resistant tumors

38 INVITED

Is there still a place for immunotherapy?

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Immunotherapy has been used for decades for the treatment in RCC. In an adjuvant setting it did not show clinical benefit. For mRCC in randomized studies, IFN-alpha has proven superiority for survival over hormonal therapy in patients with mRCC. The patients who benefited were of good WHO status (0−1) and were treated for at least 12 weeks and up to 1 year with an improved survival of several months. Interleukin-2 (IL-2) has been used in mRCC since 1985 with a substantially higher toxicity than that of IFN-alpha. Several studies have shown responses ranging from 7−27%. The optimal IL-2 regimen is not clear, but long-term (>10 years) complete responders have been achieved with high-dose bolus IL-2. However, no randomized study has been done against best supportive care. It seems that only clear cell type RCC responds to immunotherapy.
Several randomized studies have been performed to investigate the efficacy of combinations of cytokines. Patient survival was not better than survival achieved with monotherapy. No other combinations with cis-retinoic acid or 5FU have shown a clinical significant benefit, although some survival advantage has been seen. It can be concluded that immunotherapy can be beneficial in good risk mRCC patients with clear-cell type histology. This has to be seen in the era of new targetted drugs. These chronic drugs have a high stabilizing capacity, were the significance of survival benefit is still under discussion. This had to be seen against the immunotherapy strategies

Symposium (Mon, 24 Sep, 14:45−16:45)
Biological targeting for radiotherapy

39 INVITED

Imaging of the biological target

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Molecular imaging allows molecular and cellular events to be tracked in a living organism. Powerful new targeted imaging technology has become available including fMRI and PET for which specific tracers have been developed for tumor cell proliferation, metabolism, apoptosis, angiogenesis, receptor and gene expression. The long term goal of these studies is to use this new technology to stage the disease, to select the treatment for the patient (treatment individualisation), to plan treatment volumes that compensate for volumes of radioresistant disease, and to evaluate treatment efficacy (early response prediction and early detection