2.7%, p = 0.041). In the Capox-RT group, 85.7% (191/223) patients received radiotherapy on schedule and 74.9% (166/223) with concurrent chemotherapy on schedule, as did 94.1% (238/253) and 92.1% (233/353) in the Cap-RT group, respectively. Grade 3-4 acute toxicity was observed in 38.1% of patients in the Capox-RT group and in 29.2% in the Cap-RT group (p = 0.041). Grade 3-4 tenesmus was more common in the Capox-RT group than in the Cap-RT group (5.4% vs. 2.0%), as were grade 3-4 nausea (2.2% vs. 0%), grade 3-4 vomiting (1.8% vs. 0%), and grade 3-4 fatigue (3.1% vs. 0.4%).

Conclusions: The interim analysis revealed that inclusion of oxaliplatin into capecitabine based postoperative chemoradiotherapy was feasible and could decrease cumulative locoregional recurrence rate for patients with locally advanced rectal cancer.

Symposium: Future in Radiation Oncology: The way to the right central position

SP-0614
How can we help patients to make a treatment choice that fits them best? (Shared decision making)
J. J. Van Tol-Geerdink1
1Radboud University Medical Center, 874 Radiation Oncology, Nijmegen, The Netherlands

Traditionally, oncology patients are inclined to follow the treatment advice of their physician without asking too many questions. However, for many patients different treatment options are available. Each option will have its own pros and cons, which may be weighed differently by individual patients. This calls for shared decision making (SDM) and patient involvement in the treatment choice. In order to involve patients as partners in decision making, however, different steps are required. Patients should be invited to participate in the tradeoff between options. They need evidence-based information on the risks and benefits of different options presented in a structured way, preferably using visual aids. And they need to be stimulated to think about which aspects are most important to them.

When available, decision aids are useful tools to give patients evidence-based information and to help them make a personal tradeoff. Decision aids have proven to be effective, e.g. in a recent Cochrane review (2011). Knowledge increases, less patients remain undecided on the their treatment preference, more patients take an active role in decision making, and they are more aware of which treatment outcomes are most important to them. As a consequence, the treatment choice better fits their personal situation and their individual preference.

Within radiotherapy, we studied patient involvement in the choice between a lower or higher radiation dose reflecting the tradeoff between the likelihood of cure and the likelihood of serious side effects. Other radiotherapy-related choices include radiotherapy vs. surgery, radiotherapy vs. best supportive care, chemoradiotherapy vs. radiotherapy alone or conventional fractionation vs. hyper- or hypofractionation.

Some physicians may hesitate to involve cancer patients in treatment decisions. One reason may be that some doctors believe they can predict their patients preferences, so they don’t need to bother their patients with trade-offs. However, preferences for treatment and for involvement appear to be hard to predict for physicians, and even for patients themselves. Once informed, they become more active partners in decision making than they previously predicted, and their preferences can differ from what their physicians expected. Moreover, sharing information about the pros and cons of different treatment options is appreciated by the vast majority of patients, even by those who prefer to leave the ultimate decision to their physician.

Other possible barriers for SDM are the assumptions that patients are unable to make a consistent choice, that it may be a burden for patients to take responsibility for the decision or that it may induce regret over the choice later on, especially for patients with poor outcome. However, research shows that patient choices are consistent with their values and concerns. Moreover, anxiety is not increased and regret, if anything, appears to be reduced, particularly in those patients that experience poor outcome. Finally, the idea that shared decision making may be too time consuming is not confirmed by the results of recent implementation studies.

Illustrated by our research, (mis)perceptions and tips about shared decision making will be discussed.

Proffered Papers: Radiobiology 4: Novel targeted agents

OC-0615
Voxel-based perfusion normalisation in GBM patients included in a phase-I-II trial of RT/Tipifarnib combination S. Ken1, A. Deviers1, T. Fillieron2, I. Catala2, J.A. Lotterie3, V. Lubrano4, I. Berry4, P. Péran5, E. Cohen-Jonathan Moyal5, A. Laprie1
1Institut Claudius Regaud IUCT-Oncopole, Department of Radiotherapy and Medical Physics, Toulouse, France
2Institut Claudius Regaud IUCT-Oncopole, Bureau des Essais Cliniques, Toulouse, France
3Centre Hospitailier Universitaire, Purpan, Toulouse, France
4Centre Hospitailier Universitaire, Rangueil, Toulouse, France
5INSERM UMR 825, Imagerie Cérébrale et Handicaps Neurologiques, Toulouse, France

Purpose/Objective: Based on our lab results showing that the Farnesyl Transferase Inhibitor, Tipifarnib induced a vascularization normalisation, oxygenation and radiosensitisation in glioblastoma (GBM) model, we performed a phase-I-II clinical trial associating Tipifarnib with radiotherapy in GBM patients. The aim of this study was to assess by dynamic susceptibility contrast MRI (DSC-MRI) the effect the combined treatment on tumor perfusion.

Materials and Methods: Eighteen patients with newly diagnosed GBM were included in a phase-I-II clinical trial associating RT with Tipifarnib, they underwent conventional anatomical MR imaging and DSC-MRI before and two months after treatment (M0 and M2 respectively). Anatomical volumes of interest (VOIs) were defined by contrast-enhanced (CE) regions on post-gadolinium based T1 MR images and areas of hyper-intense signal on T2 MR images. Perfusion changes between M0 and M2 were assessed by measuring the variation of the median relative CBV (rCBV) inside these anatomical VOIs. Another voxel by voxel analysis of CBV values classified 138,646 tumor voxels (inside the CE VOI) into High, Normal_ and Low_CBV_Tumor according to the distribution of CBV in the contralateral normal tissue: for CBV value higher than the 95th percentile of the normal contralateral distribution, the voxel was classified in the High_CBV_Tumor class (red voxels); for CBV value between the 25th and the 75th percentile, the voxel was classified in the Normal_CBV_Tumor class (green voxels) and for CBV value below the 25th percentile, the voxel was classified in the Low_CBV_Tumor class (blue voxels). All
classes of CBV\textsubscript{TUMOR} were reported to the total CBV\textsubscript{TUMOR} to show volume variations in percentage.

**Results:** Variations of median rCBV between M0 and M2 were different for two groups of patients: rCBV increased when initial rCBV was <1.0 (Group\textsubscript{rCBV\_M0<1}) and rCBV decreased when initial rCBV was >=1.0 (Group\textsubscript{rCBV\_M0>1}), this was statistically significant (p<0.013). Mapping of color-coded voxels between M0 and M2 provided additional spatial and quantitative information about tumor perfusion: Group\textsubscript{rCBV\_M0>1} presented a significant decrease of High\textsubscript{CBV\_TUMOR} volume (p=0.015) simultaneously with a decrease of Low\textsubscript{CBV\_TUMOR} volume. Two examples of these CBV\textsubscript{TUMOR} volumes variations between M0 and M2 are illustrated for a patient of each group over their anatomical MRI, respectively Fig1A for a patient of Group\textsubscript{rCBV\_M0>1} and Fig1B for a patient of Group\textsubscript{rCBV\_M0<1}.

**Conclusions:** Pre and post-treatment CBV measurements with DSC-MRI characterized tumor perfusion evolution in GBM patients treated with RT combined to Tepofarnib; showing variations in favour of tumor perfusion normalisation in agreement with our pre-clinical results of vascular normalisation.

**OC-0616** Enhancing the efficacy of lung cancer treatment via Notch receptor targeting

V.S.I. Sosa Iglesias\textsuperscript{1}, J.T. Theys\textsuperscript{1}, S.Y. Yahyanejad\textsuperscript{1}, L.D. Dubois\textsuperscript{1}, M.V. Vooijs\textsuperscript{1}

\textsuperscript{1}University of Maastricht FHML, Radiation Oncology, Maastricht, The Netherlands

**Purpose/Objective:** Lung cancer is the leading cause of cancer death worldwide and alternative treatment strategies are needed to eradicate non-responsive or recurrent tumor cells. The Notch signaling pathway plays a key role during normal lung development and is frequently deregulated in non small cell lung cancer (NSCLC) making it a potentially attractive therapeutic target. We and others have shown that in NSCLC xenografts high Notch activity is correlated with faster proliferation, higher hypoxic fraction and resistance to radiotherapy. These findings have led us to further investigate the interactions between standard of care treatments (chemo/radiotherapy) in conjunction with Notch inhibitors both in vitro and in vivo.

**Materials and Methods:** Monolayer cultures of diverse lung cell lines were used to determine the IC50 value by measuring the metabolic activity of the acid phosphotase enzyme in cells after treatment with a range of chemotherapeutic agents both as a monotherapy and in combination with Notch receptor inhibition. In addition, the effect of single and combined treatment schedules was tested using a quantitative spheroid growth delay assay. In vivo evaluation of therapeutic efficacy of the combination treatment before mentioned has been initiated using a xenograft lung cancer model.

**Results:** IC50 value analysis of various chemotherapeutic agents revealed striking differences in responses across cell lines. The human lung cancer cell line H460 was more sensitive to etoposide, docetaxel and paclitaxel than different mouse cell lines deriving from mouse tumors bearing Kras and p53 mutations with different metastasizing potentialities (344P; 344SQ and 393P) but equally sensitive to cisplatin than 344P and 344SQ cell lines. The 393P cell line derived from a primary tumor that didn't metastasize was more resistant than the rest of the cell lines to cisplatin and paclitaxel. Interestingly, although Notch inhibition alone had no effect upon cell growth after 72h of treatment, the combination with either cisplatin or etoposide resulted in a growth delay with respect to the monotherapy treatment. In spheroid cultures of H460 cells the combination of 2.5\mu M cisplatin with 4 \mu M DAPT (Notch inhibitor) instigated more growth delay than the monotherapy treatments. Experiments to quantify the growth delay when also radiation is given are underway. In addition, in vivo experiments are ongoing to investigate whether the synergistic drug combination found in vitro also applies for an in vivo model. Two different doses of cisplatin were tested in vivo whereby 3.5mg/kg had a good efficacy and better tolerance than 7mg/kg and therefore will be used to test the combination treatment with the dose of Notch inhibitor that yields an optimal response as monotherapy and with radiation.

**Conclusions:** The addition of Notch inhibitors to cisplatin (chemotherapeutic used to treat lung cancer patients) leads to an enhanced treatment response in vitro and may lead to one in vivo as well.

**OC-0617** The PARP inhibitor olaparib is effective as radiosensitizer at 10-fold lower doses than as single agent

R. De Haan\textsuperscript{1}, C.V.M. Verhagen\textsuperscript{2}, F. Hageman\textsuperscript{3}, T. Oostendorp\textsuperscript{4}, A. Di Carlo\textsuperscript{1}, M.J. O'Connor\textsuperscript{3}, J. Jonkers\textsuperscript{4}, B. Van Triest\textsuperscript{1}, M.W.M. Van den Brekel\textsuperscript{1}, M. Verheij\textsuperscript{1}, C. Vens\textsuperscript{1}

\textsuperscript{1}The Netherlands Cancer Institute, Division of Radiation Oncology and Division of Biological Stress Response, Amsterdam, The Netherlands
\textsuperscript{2}The Netherlands Cancer Institute, Division of Biological Stress Response, Amsterdam, The Netherlands
\textsuperscript{3}AstraZeneca, DNA Damage Response Strategic Biology Area, Macclesfield, United Kingdom
\textsuperscript{4}The Netherlands Cancer Institute, Division of Molecular Pathology, Amsterdam, The Netherlands

**Purpose/Objective:** Novel targeted agents, such as PARP inhibitors, are combined with radiotherapy (RT) to induce tumor-specific radiosensitization. Safety and tolerability of olaparib in combination with RT is currently tested in several clinical phase 1 trials. When used as single agent in clinic, olaparib is well tolerated and has proven anti-tumor efficacy in BRCA1 and 2 mutation carriers. As the mechanisms of action of olaparib as radiosensitizer or as single agent may differ, also the dose range of tolerability and effectiveness might differ. In this in vitro study, we compared efficacy of