and bad (28%). The data were collected prospectively for 42% of patients. Rectal toxicity was analyzed according to the SOMALENT classification (> Grade 2) and rectal bleeding (at least once episode) at 2, 3, 4 and 5 years. The effects of pts characteristics, DVH (including mean dose) and NTCP models on rectal toxicity at the different follow-ups were assessed using logistic regression (univariate and multivariate analysis). A total of 6 NTCP models were tested: Lyman Kutcher Burman (LKB), logit EUD, Poisson EUD, Kallman, Schultheiss and Parallel models. The parameters of the models were identified using the MATLAB Genetic Algorithm Toolbox and constrained optimization. The performance for predicting toxicity of the models was performed using Efron's pseudo R squared.

Results: Median follow-up was 60 months (range: 6 to 154). Two-, 3-, 4- and 5-year grade >2 toxicity rates were: 15%, 21%, 25% and 30%, respectively. Two-, 3-, 4- and 5-year rectal bleeding rates were: 21%, 28%, 32% and 38%, respectively. Univariate analysis shown following parameters as significant predictor of 4-year grade >2 toxicity: total prescription dose, V_{71} to V_{73} and maximal rectal dose. In multivariate analysis, the remaining factors were total dose, V_{72} and V_{73}. The table shows the parameters of the NTCP models. The NTCP models which probability values are significantly related with bladder toxicities are: LKB, Logit EUD and Poisson EUD models. The model having the better predictive capability is Poisson EUD model.

Conclusions: Both, some DVH parameters and three NTCP models (Poisson EUD model being the most predictive) are useful to assess rectal toxicity and could be used as constrains in IMRT planning.

Table: NTCP of 4 Year rectal toxicity (grade $\geqslant$2)

Model	TD_{50} (Gy)	Volume Effective Factor	Slope Factor	Log-Likelihood (p value)
LKB	79.14	n = 0.0025	m = 0.2705	159.05 (0.0022)
LogitEUD	80.57	n = 0.0063	k = 9.5959	159.08 (0.0022)
PoissonEUD	81.50	n = 0.0063	γ = 2.1618	158.95 (0.0018)

7007 POSTER DISCUSSION

Predictive Models of Bladder Toxicity in Prostate Cancer Radiotherapy

J. Zhu[1], A. Simon[2], J.D. Ospina[2], E. Le Prisé[3], A. Bossi[4], C. Chira[3], K. Gnep[3], V. Beckendorf[5], V. Polet[5], R. De Crevoisier[6]. [1]*Southeast University, Laboratory of Image Science and Technology, Nanjing, China;* [2]*INSERM U642, Laboratoire Traitement du Signal et de l'Image, Rennes, France;* [3]*Centre Eugène Marquis, Département de Radiothérapie, Rennes, France;* [4]*Institut Gustave Roussy, Département de Radiothérapie, Villejuif, France;* [5]*Centre Alexis Vautrin, Département de Radiothérapie, Nancy, France;* [6]*Centre Eugène Marquis INSERM U642, Département de Radiothérapie, Rennes, France*

Background: In case of prostate 3D conformal radiotherapy (3DCRT), the objectives were:

– To identify patients and treatment predictors of bladder toxicity;
– To compare the performance of different Normal Tissue Complication Probability (NTCP) models for predicting bladder toxicity.

Materials and Methods: A total of 436 patients (pts) received 3DCRT for localized prostate cancer to a median total dose of 78 Gy (range: 70 to 80 Gy), 2 Gy/fraction. Pts were selected based on the availability of dose-volume histogram (DVH). Median age was 67 years (45−78). History of abdominal or pelvic surgery, anticoagulant therapy (ACT) and diabetes were observed in 30%, 15% and 6% of pts, respectively. Tumour prognostic groups (D'Amico classification) were: good (7%), medium (65%) and bad (28%). The data were collected prospectively for 42% of patients. Bladder toxicity was analyzed according to the SOMALENT classification ($\geqslant$ Grade 2) and bladder bleeding (at least once episode) at 2, 3, 4 and 5 years. The effects of pts characteristics, DVH (including mean dose) and NTCP models on bladder toxicity at the different follow-ups were assessed using logistic regression (univariate and multivariate analysis). A total of 6 NTCP models were tested: Lyman Kutcher Burman (LKB), logit EUD, Poisson EUD, Kallman, Schultheiss and Parallel models. The parameters of the models were using the MATLAB Genetic Algorithm Toolbox and constrained optimization. The performance for predicting toxicity of the models was performed using Efron's pseudo R squared.

Results: Median follow-up was 60 months (range: 6 to 154). Two-, 3-, 4- and 5-year grade $\geqslant$2 toxicity rates were: 15%, 19%, 24% and 30%, respectively. Two-, 3-, 4- and 5-year bladder bleeding rates were: 6%, 9%, 11% and 16%, respectively. Univariate analysis shown following parameters as significant predictor of 4-year grade $\geqslant$2 toxicity: diabetes, total prescription dose and maximal bladder dose (none of the DVH values). In multivariate analysis, the remaining factor was the total dose. The table shows the parameters of the significant NTCP models.

The NTCP models which probability values are significantly related with rectal toxicities are: LKB, Logit EUD, Poisson EUD and Schultheiss models. The model having the better predictive capability is LKB model.

Conclusions: NTCP models (LKB model being the most predictive) are useful to assess bladder toxicity and could be used as constrains in IMRT planning.

NTCP of 4 Year bladder toxicity (grade $\geqslant$2)

Model	TD_{50} (Gy)	Volume Effective Factor	Slope Factor	Log-Likelihood (p value)
LKB	80.56	n = 0.0920	m = 0.3641	158.12 (0.0038)
LogitEUD	81.00	n = 0.0431	k = 7.6206	157.91 (0.0049)
PoissonEUD	82.19	n = 0.0409	γ = 1.7510	157.88 (0.0045)
Schultheiss	71.38	–	k = 8.2548	160.69 (0.0089)

7008 POSTER DISCUSSION

Twenty-four-month Safety Data From Phase II Studies of Radium-223 Chloride, a First-in-class Alpha-pharmaceutical With a Highly Favorable Safety Profile for Patients With Castration-resistant Prostate Cancer (CRPC) and Bone Metastases

S. Nilsson[1], I. Haugen[1], A. Aksnes[1], C.G. O'Bryan-Tear[1], C. Parker[2]. [1]*Algeta ASA, Clinical Department, Oslo, Norway;* [2]*The Royal Marsden Hospital, Academic Urology Unit, Sutton, United Kingdom*

Background: Radium-223 chloride (^{223}Ra; Alpharadin™) is a first-in-class alpha-pharmaceutical with a potent, highly targeted antitumour effect on bone metastases. Phase II trials assessed the safety and efficacy of ^{223}Ra in patients (pts) with CRPC and bone metastases. Here we report long-term safety data from the end of the treatment period until 24 months after the first injection of ^{223}Ra.

Methods: Two double-blind, dose-response phase II trials (BC1−03 [NCT00667199], BC1−04 [NCT00337155]) and 1 double-blind, placebo-controlled phase II trial (BC1−02 [NCT00459654]) of ^{223}Ra were conducted in 286 pts with CRPC and bone metastases (255 pts received ^{223}Ra;100, 122, and 33 pts in BC1−03, BC1−04 and BC1−02, respectively). Doses varied from 5 to 100 kBq/kg (single [BC1−03] and repeated injections [BC1−02 and BC1−04]). Follow-up safety assessments were performed at months 6, 9, 12, 18, and 24 and included treatment-related adverse events (AEs), hematology, clinical chemistry, potential long-term toxicity, and death. Twenty-four month safety data are available for all 3 studies.

Results: A total of 159 pts were included in this analysis. No pts reported any treatment-related serious AEs during follow-up to 24 months. One patient had mild diarrhea 2 days after receiving an optional second injection of 50 kBq/kg ^{223}Ra at the start of follow-up; it was reported as probably related to the last ^{223}Ra injection. One patient reported lumbar pain after 24 weeks (only treatment-related AEs were reported during follow-up). CTC grade 4 hematologic toxicity was seen in 1 patient each for platelets, neutrophils, WBC, and hemoglobin. Across all studies, 7 pts experienced CTC grade 3 anemia, 5 pts grade 3 thrombocytopenia, and 3 pts grade 3 neutropenia. The BC1−02 study showed no statistically significant difference in hematologic parameters between the ^{223}Ra and placebo groups during follow-up. No patient reported a secondary diagnosis of acute myelogenous leukemia, myelodysplastic syndrome, aplastic anemia, or primary bone cancer. No signs of renal or hepatic toxicity were observed. The frequency and cause of death during follow-up were as anticipated for pts with metastatic CRPC.

Conclusion: Safety data from the 24-month follow-up period support previous findings of the highly favorable safety profile of ^{223}Ra in pts with CRPC and bone metastases. A randomized phase III study, ALSYMPCA, is ongoing worldwide with overall survival as the primary endpoint.

7009 POSTER DISCUSSION

Sensitivity and Specifity to Detect Local Recurrent Prostate Cancer Using Dynamic Contrast Enhanced (DCE) MRI Without Endorectal Coil and MRI Patterns of Post-prostatectomy Recurrence and of Its Response to Salvage Radiotherapy

H.C. Rischke[1], U. Nestle[1], N. Volegova-Neher[1], K. Henne[1], S. Kirste[1], S. Knippen[1], W. Schultze-Seemann[2], A.L. Grosu[1]. [1]*Universitätsklinikum Freiburg, Radiation Oncology, Freiburg, Germany;* [2]*Universitätsklinikum Freiburg, Urology, Freiburg, Germany*

Purpose: To determine sensitivity and specifity of dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) without endorectal coil