vitro. Co-expression of Dlx2 activated p107-luciferase promoter gene expression in vitro. p107 expression was reduced in the Dlx1/Dlx2 DKO mouse retina at E18.5. DLX2 was expressed in the nuclei of Chx10:Rb-p107 conditional DKO retinoblastoma as well as in almost all human retinoblastoma tissues we studied.
Conclusions: The homeodomain transcription factor DLX2 directly activates expression of the tumour suppressor p107, a member of the Rb pocket protein family essential for cell cycle regulation. Expression of DLX2 in both mouse and human retinoblastoma supports that these developmental tumours are partially differentiated and contributes to our knowledge regarding the cell of origin. Future studies will determine whether modulation of DLX2 expression regulates cell proliferation and differentiation of retinoblastoma.

O-110

IMPACT OF RB1 MUTATION PRENATAL DIAGNOSIS ON CHILDREN AT RISK FOR RETINOBLASTOMA

B. Gallie[1], H. Dimaras[1], H.S.L. Chan[2], E. Héon[1], J. Sutherland[1], M. Day[1], M. Day[1]

[1]Ophthalmology and Vision Science, The Hospital for Sick Children, Toronto, Canada; [2]Division Hematology Oncology Dept Paediatrics, The Hospital for Sick Children, Toronto, Canada

Objectives: Canadian Guidelines for Retinoblastoma Care[1] recommend testing infants for their affected parent's *RB1* mutation prenatally or at birth; infants carrying the *RB1* mutation may be delivered late pre-term [HD1] or near-term (36, 37 weeks gestation) to optimize opportunities for minimal impact treatment of small tumors. We evaluate effects of gestational age at first eye examination on outcomes of children carrying an *RB1* mutation.
Methods: We retrospectively studied infants carrying their family's *RB1* mutation, born between 1 June 1996 and 31 May 2013 and treated at SickKids. Information collected included: affected parent; sex; gestational age at birth, *RB1* testing and first eye exam; pregnancy or perinatal complications; type of sample tested and *RB1* mutation; locations of first and subsequent tumors; International Intraocular Retinoblastoma Classification and Tumour Node Metastasis staging; treatments delivered; last followup date; and overall and visual outcomes.
Results: Twenty infants carried their parent's *RB1* mutation, detected prenatally in 12 and after birth in 8. Nine were tested prenatally and electively delivered at 36-37 weeks gestation and 3 were spontaneously premature. All infants not tested prenatally were born at term. All newborn infants had weekly eye examinations. Vision-threatening tumors were present at birth in 25% (3/12) of infants delivered early or born prematurely and 75% (6/8) of full-term infants; posterior tumors appeared age 1 to 6 months in 9 infants. All patients eventually developed bilateral retinoblastoma. Good vision was maintained in all children born early; treatments included focal therapy (all) and later chemotherapy (5), stereotactic radiation and enucleation of one eye due to chemotherapy intolerance (1). Full-term infants received focal therapy (8), chemotherapy (5), and enucleation of one eye (2); bilateral macular tumors blinded one child.
Conclusion
Prenatal molecular detection and early delivery facilitated optimal outcomes.
1. National Retinoblastoma Strategy Canadian Guidelines for Care. Canadian Journal of Ophthalmology. 2009;44:S1-88.

O-111

A PROSPECTIVE SINGLE INSTITUTION TRIAL USING TOPOTECAN BASED CHEMOTHERAPY FOR THE TREATMENT OF BILATERAL INTRAOCULAR RETINOBLASTOMA

R. Brennan[1], M.W. Wilson[2], S. Mao[3], J. Wu[3], I. Qaddoumi[1], C. Rodriguez-Galindo[4]

[1]Oncology, St. Jude Children's Research Hospital, Memphis, USA; [2]Ophthalmology, University of Tennessee Health Science Center, Memphis, USA; [3]Biostatistics, St. Jude Children's Research Hospital, Memphis, USA; [4]Oncology, Dana Farber Cancer Institute, Boston, USA

Objectives: To evaluate efficacy of systemic chemo-reduction using topotecan for advanced intraocular retinoblastoma.
Methods: 27 newly diagnosed bilateral retinoblastoma patients (14 males, median age 7.9 months), worse eye Reese- Ellsworth (RE) group IV-V, received 11 cycles of chemotherapy: topotecan and vincristine (TV) x 2 followed by three alternating courses of carboplatin and vincristine x 2 and TV x 1. Intensive focal therapy was applied after the first 2 cycles. Event free survival (EFS) was defined as avoidance of external beam radiation (EBRT) and enucleation.
Results: Of 54 eyes, 42 were RE IV-V and 37 were International Classification (IC) C-E. 24 patients (89%) completed all prescribed chemotherapy; one was removed due to persistent viral infection and two had progressive disease requiring EBRT. All eyes received focal therapy. Seven patients received subconjunctival carboplatin during therapy, and six received plaque brachytherapy during follow-up. Eleven eyes were enucleated: one at diagnosis, nine with progressive disease including three eyes treated with EBRT, and one which developed neovascular glaucoma. At 8 years, cumulative incidence of EBRT was 2.4% (SE ± 2.4) and EFS for patients was 66.7% (SE ± 38.5). Ocular survival for RE group IV-V eyes was 76.2% (SE ± 26.3) and 70% (SE+ 27.0) for IC group D-E eyes. All patients experienced thrombocytopenia (41 episodes in 275 courses, 15%). There were 29 episodes of febrile neutropenia (10%). Fifteen patients had a documented source of infection (40% viral etiology). Grade 3 diarrhea was present in 9/27 patients, and one patient reacted to carboplatin. All patients are alive with median follow up was 7.4 years.
Conclusions: Topotecan combined with vincristine, carboplatin and aggressive focal therapies is an effective regimen for the treatment of advanced retinoblastoma (RE IV-V) that avoids radiation and results in globe salvage with measurable vision. Toxicities were anticipated and managed with appropriate supportive care.

O-112

TREATMENT OF RECURRENT OR PROGRESSIVE INTRAOCULAR RETINOBLASTOMA: PRELIMINARY RESULTS OF A NATIONAL PHASE II STUDY OF THE SWISS PEDIATRIC ONCOLOGY GROUP

M. Beck Popovic[1], S. Binaghi[2], M.C. Gaillard[3], M. Diezi[4], E. Garcia[4], S. Houghton[3], M.T. Galley[1], M. Cornu[1], S. Pampallona[5], F. Munier[3]

[1]Pediatric Hematology Oncology Unit, CHUV-University Hospital, Lausanne, Switzerland; [2]Interventional Radiology, CHUV-University Hospital, Lausanne, Switzerland; [3]Jules Gonin Eye Hospital, University Hospital, Lausanne, Switzerland; [4]Pediatric Hematology-Oncology Unit, CHUV-University Hospital, Lausanne, Switzerland; [5]Statistics for Medicine, forMed, Evolene, Switzerland

Objectives: To determine the effectiveness and safety of injections of Melphalan via the ophthalmic artery (SOAC), or into the vitreous cavity (IVC), or of periocular Topotecan (POT), as salvage therapies for recurrent/progressive retinoblastoma (Rb) according to the site of recurrence/progression. To evaluate the eye preservation rate after 3 courses of SOAC, 3 courses of IVC, 2 courses of POT (no enucleation and/or radiotherapy).
Methods: National single arm phase II prospective study including patients (pts) with recurrent/progressive Rb between 6 months and 15 years of age after failure to prior treatment (chemoreduction/focal therapy, plaque therapy, external beam radiation), with RetCam images and ultrasound biomicroscopy for identification of tumor-free meridian mandatory for IVC. Each patient was enrolled and evaluated only for one treatment arm. Response was evaluated after each treatment course for retinal tumors and/or vitreous seeds. Treatment was stopped at any time in case of progression, toxicity or parental refusal.
Results: Thirty-one pts were registered, 14 (4 with unilateral and 10 with bilateral disease) were eligible after failure to prior chemotherapy only (12) or chemotherapy/radiotherapy (2). Salvage treatment consisted of SOAC in 7, IVC in 5 and POT in 2 pts. Response was favorable in 3/7 SOAC, 5/5 IVC and 2/2 POT administrations. There was no enucleation or radiotherapy after a median follow-up of 7 months (1-16). Six out of 14 pts needed further treatment, 5 in the same eye (SOAC 1, IVC 1, combined SOAC/IVC 3), 1 in the contralateral eye (combined). Ocular hemorrhage in 2/14 eyes after SOAC was the worst adverse event observed, treated successfully with anti-VEGF.
Conclusions: In heavily pretreated Rb patients SOAC, IVC and POT are efficient in treating recurrent/progressive disease and preventing enucleation and/or radiotherapy. However, almost half of the treated eyes need further treatment for disease control. Treatment combinations should be considered in future.

O-113

EFFICACY OF SECOND COURSE OPHTHALMIC ARTERY CHEMOSURGERY FOR RETINOBLASTOMA THAT RECURS FOLLOWING PRIOR OPHTHALMIC ARTERY CHEMOSURGERY

L.J. Dunkel[1], Y.P. Gobin[2], B.P. Marr[3], I. Tendler[4], S.E. Brodie[5], D.H. Abramson[3], J.H. Francis[6]

[1]Pediatrics, Memorial Sloan Kettering Cancer Center and New York Presbyterian Hospital Weill Cornell Medical College, New York, USA; [2]Neurosurgery, Memorial Sloan Kettering Cancer Center and New York Presbyterian Hospital Weill Cornell Medical College, New York, USA; [3]Ophthalmology, Memorial Sloan Kettering Cancer Center and New York Presbyterian Hospital Weill Cornell Medical College, New York, USA; [4]Pediatrics, Memorial Sloan Kettering Cancer Center, New York, USA; [5]Ophthalmology, Memorial Sloan Kettering Cancer Center and Mount Sinai, New York, USA; [6]Ophthalmology, Memorial Sloan Kettering Cancer Center, New York, USA

Objectives: Melphalan-based ophthalmic artery chemosurgery (OAC) has been highly effective for intra-ocular retinoblastoma, but some patients who achieve remission develop recurrence following completion of therapy. We aimed to evaluate the efficacy of second course OAC for such patients.
Methods: Single-arm, retrospective study of 32 eyes that underwent OAC at our centers between May 2006 and July 2013 and achieved remission, but suffered intra-ocular retinoblastoma recurrence at least 2 months off-therapy. Outcome measurements included Kaplan-Meier estimates of ocular progression-free survival (PFS) and ocular survival, and the Mantel-Cox test was used to compare curves.
Results: The eyes previously received a mean of 3.1 first course OAC infusions and developed off-therapy disease recurrence at a median of 4.4 months following completion of initial OAC.