Journal Club: The Lightning Rounds

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Introduction

Journal Club: The Lightning Rounds is a synopsis of current literature in Pediatric hematology & oncology. The articles have been selected from clinical and scientific journals, and represent high impact research that may influence the current and future practice of pediatric hematologist and oncologists.

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Prevention of conversion to abnormal transcranial Doppler with hydroxyurea in sickle cell anemia: A Phase III international randomized clinical trial.

Hankins JS (2015), American Journal of Hematology (Link to Abstract)

Cerebrovascular stroke is a known complication of sickle cell disease. Previous studies have established monitoring transcranial doppler ultrasound velocities as an effective way to monitor the risk of stroke in these patients. Currently, treatment is initiated for those children at highest risk of stroke (TCD velocity >200 cm/sec), while those with conditional velocities (170-199 cm/sec) are observed. This is a prospective randomized control trial comparing TCD ultrasound velocities in sickle cell patients with conditional TCD velocities who were and were not treated with hydroxyurea.

38 children were enrolled on the trial. There was a significant difference in conversion of conditional TCD velocities to abnormal or high risk velocities (>200 cm/sec) between the treatment and control arms by post hoc analysis (9% in the treatment group compared and 47% in the control group, respectively, P=0.02), though no strokes occurred in either group. In addition, the treatment group showed a significant decrease in their mean TCD velocities (P=0.02). Unfortunately, the study had to be closed early due to difficulties with patient accrual, and therefore the numbers were insufficient to prove significant prevention of progression by intention-to-treat analysis.

Successful matched sibling donor marrow transplantation following reduced intensity conditioning in children with hemoglobinopathies.

King, AA (2015), American Journal of Hematology (Link to Abstract)

Hematopoietic stem cell transplantation (HSCT) is curative for patients with hemoglobinopathies, but is often delayed or avoided because of the significant risks associated with it, particularly those associated to the myeloablative conditioning. The authors initiated a prospective multi-center trial of reduced intensity conditioning (RIC) with Alemtuzumab/ Fludarabine/ Melphalan in 52 children with hemoglobinopathies (sickles cell disease and thalassemia) who were to undergo HSCT with a matched sibling donor marrow or cord blood graft. Event free survival following RIC was 92%, which was comparable to myeloablative transplants (>85%), proving non-inferiority. Successful engraftment was maintained after withdrawal of immunosuppression in all but one case, and all cases with successful engraftment remained transfusion independent and without complications of their initial condition.

- Reduced intensity conditioning is emerging as an alternative option for patients with hemoglobinopathies undergoing matched sibling bone marrow transplantation.
Transfusion of fresher vs older red blood cells in hospitalized patients: a systematic review and meta-analysis.

Alexander P (2016), Blood (Link to abstract)

This meta-analysis looked at 12 trials that enrolled 5229 participants, 6 compared fresher RBCs with older RBCs and 6 compared fresher RBCs with the local standard practice. All of the studies were deemed to be of good quality with low risk of bias. There appeared to be low or no effect of the age of RBCs on mortality. Interestingly, fresher RBC seemed to be associated with higher rate of nosocomial infections. Although the definitions of “new” or “old” blood were varied, the statistical heterogeneity between the studies was low.

- There is no rationale to favor fresher RBCs over older ones in terms of mortality. The increased risk of nosocomial infections with fresher RBCs is surprising and should be further analyzed. This well designed and executed trial may finally end the debate around using fresh RBCs.

Sirolimus is effective in relapsed/refractory autoimmune cytopenias: results of a prospective multi-institutional trial.

Bride KL (2016) Blood (Link to abstract)

Thirty patients aged 5 months to 19 years with refractory or relapsed autoimmune cytopenias were included and treated with sirolimus as monotherapy (target trough 5-15ng/mL). All children with autoimmune lymphoproliferative syndrome (ALPS) showed durable complete remission (CR) after 1-3 months therapy. 8/12 patients with other autoimmune cytopenias (Evans syndrome, systemic Lupus erythematosus, and CVID associated cytopenias) achieved CR. 2/6 children with unilineage cytopenias responded to treatment. Responding patients were continued treatment with sirolimus a median of two years (range 1-4.5years). The most common toxicity was low grade mucositis that occurred early and resolved with continued treatment.

- This report establishes sirolimus as a treatment option in ALPS with rapid durable response in all patients treated in this cohort. Refractory/ relapsed multilineage cytopenias also seem to be responsive. However, unilineage cytopenias are less effectively treated.
TALEN-mediated genetic inactivation of the glucocorticoid receptor in cytomegalovirus-specific T cells

Menger L (2015) Blood (Link to abstract)

T-cells control Cytomegalovirus (CMV) infection/ reactivation after allogeneic hematopoietic stem cell transplantation (HSCT). T- cell therapy can be used to control CMV replication after HSCT but patients with graft-versus-host disease (GVHD) on steroids are usually not given this treatment due to the fear of suppression and inactivation of transferred T cells by steroids. Genetic disruption using electroporation of transcription activator–like effector nuclease (TALEN) messenger RNA was used by the authors to interfere with the glucocorticoid receptor (GR) gene on T cells. In vitro assays showed that CMV-specific CD8+ T cells retained specific killing of target cells.

- This report provides evidence that manipulation of the glucocorticoid receptor of genetically engineered T cells could induce resistance to steroids of these cells and therefore overcome the issues with glucocorticoid treatment and T cell therapies.

Clotting Factor Product Administration and Same-day Occurrence of Thrombotic Events, as Recorded in a Large Healthcare Database During 2008-2013

Ekezue, BF (2015), Journal of Thrombosis and Haemostasis (Link to abstract)

This study utilized Blue Cross’ database (which processes all claims for people who hold that insurance) to see which patients were exposed to clotting factor products and how many of them had VTEs on the same day as the administration of the factor. They found significantly more VTEs in patients who did not have a congenital hemophilia who received factor. Although the numbers were smaller, this trend also held true in the pediatric age group. The highest risk was with increased age and with the use of Benefix or factor VIIa.

- This retrospective study seems to argue against the use of clotting factors off-label. Bear in mind, however, that many non-hemophilia patients receiving factors are likely to be sick and prone to clots for a variety of reasons – not the least of which is being on extracorporeal life support.
Escalation to High-Dose Defibrotide in Patients with Hepatic Veno-Occlusive Disease

Triplett BM (2015), Biology of Blood and Marrow Transplantation (Link to abstract)

Defibrotide is considered to be a safe and effective treatment for hepatic VOD at doses of 25 mg/kg/day. In this prospective clinical trial, 34 patients received escalating doses of up to 110 mg/kg/day of defibrotide. There was no increased toxicity and no increased bleeding episodes for doses up to 100 mg/kg/day. Increased toxicity and bleeding were observed in doses of 110 mg/kg/day (n=5 patients treated with this dose). However, the outcomes of treatment with escalated doses were similar to results from previous cohorts of patients who were treated with standard defibrotide doses.

❖ This study suggests that escalation to higher doses of defibrotide is safe, but not more effective than standard dosing.

Effect of Transfusion of Red Blood Cells With Longer vs Shorter Storage Duration on Elevated Blood Lactate Levels in Children With Severe Anemia

Aggrey Dhabangi (2015), JAMA (Link to abstract)

290 Children with severe anemia and lactic acidosis were analyzed in this study after receiving red blood cell transfusions. The authors found that RBC units with longer storage duration (25-35 days) were not inferior to RBC units stored for up to 10 days as measured either by resolution of lactic acidosis at 8 hours (primary outcome measure), or by secondary outcomes defined by improvement in clinical symptoms, normalization of vital signs, correction of laboratory abnormalities, and improvement in cerebral tissue oxygen saturation.

❖ Longer storage duration of red blood cells does not affect the outcome in children with severe anemia in terms of resolution of clinical and laboratory parameters.

REVIEWS/ PERSPECTIVES

Improving evidence on anticoagulant therapies for venous thromboembolism in children: key challenges and opportunities

Goldenberg NA (2015) Blood (Link to abstract)

International Society on Thrombosis and Haemostasis Core Curriculum Project: Core Competencies in Clinical Thrombosis and Hemostasis

McLintock, C, 2016, Journal of Thrombosis and Haemostasis (Link to abstract)
Identification of the Ki-1 antigen (CD30) as a novel therapeutic target in systemic mastocytosis

Blatt, K (2015) Blood (Link to abstract)

Brentuximab vedotin (BV), a chimeric antibody linked to an anti-tubulin agent targets CD-30 or Ki1 antigen. BV has been used in Hodgkin lymphoma and anaplastic large-cell lymphoma (ALCL) in refractory/relapsed patients with some success. This article shows that CD30 is expressed in about 50% of patients with aggressive systemic mastocytosis or mastocytic leukemia but only in 12% with indolent disease. The authors showed that BV inhibits CD30 expressing cells in vitro and in vivo mouse engraftment models. The effect of BV was enhanced when given with a drug (PKC412) targeting the most common gene mutation in mastocytosis KIT D816V.

- This study suggests that Brentuximab vedotin might be used in systemic mastocytosis with advanced disease.

The effect of donor characteristics on survival after unrelated donor transplantation for hematologic malignancy

Kollmann C (2016) Blood (Link to abstract)

6349 hematopoietic stem cell transplantation (HSCT) donor-recipient pairs (from 1988 to 2006) were examined for clinical and demographic predictors of outcome. The findings were validated in a second cohort of 4690 donor-recipient pairs (years 2007 to 2011). The authors found older donor age to be associated with lower survival in both cohorts. For every 10-year increment in donor age, there was a 5.5% increase in the hazard ratio for overall mortality. Similarly, HLA-matching was correlated with survival. In contrast, sex, parity of donor, and CMV serostatus were not associated with survival. ABO match seemed to have a modest impact on survival.

- This report further strengthens the association between older age of HSCT donor and lower survival as earlier suggested (http://www.bloodjournal.org/content/98/7/2043). In contrast to other reports (http://www.ncbi.nlm.nih.gov/pubmed/19642176), this analysis did not find an association between sex of donors and outcome.
Alemtuzumab levels impact acute GVHD, mixed chimerism, and lymphocyte recovery following alemtuzumab, fludarabine, and melphalan RIC HCT

Marsh RA, 2016, Blood (Link to abstract)

Hematopoietic stem cell transplantation (HSCT) data from 105 patients who underwent conditioning with a reduced intensity (RIC) protocol using alemtuzumab, fludarabine, and melphalan was collected. Alemtuzumab levels were measured peri HSCT. The authors found a correlation of lower alemtuzumab levels with higher incidence of: acute GVHD, full donor chimerism, faster lymphocyte recovery by day +30. The authors concluded that an optimal alemtuzumab level on day 0 would be in the therapeutic range of 0.2 to 0.4 μ leve.

This report correlates alemtuzumab levels to acute GVHD, donor chimerism, and lymphocyte recovery and suggests to perform targeted drug monitoring trials to test their hypothesis of optimal alemtuzumab levels in RIC HSCT.

Genome-wide surveillance of mismatched alleles for graft-versus-host disease in stem cell transplantation.

Sato-Otsubo A, 2015, Blood (Link to abstract)

The authors performed a genome-wide association study (GWAS) on 1589 individuals with bone marrow stem cell transplantation to identify minor histocompatibility antigen loci mismatched between donors and recipients associated with acute graft versus host disease (aGVHD). All individuals were transplanted with matched grafts on the HLA-A, -B, -C, -DRB1, and -DQB1 loci. They tested their approach on cases with DPB1 mismatch and successfully found a correlation of mismatch and aGVHD occurrence. Three new loci were identified with one within the KRAS gene harboring the strongest correlation. Unfortunately, the authors do not discuss the possible mechanism implicated with this locus variant in GVHD occurrence. Furthermore, the study was performed on a homogeneous Japanese cohort and might not be applicable to other ethnicities.

Another application of GWAS to identify possible genetic variants associated with clinical features – potentially rendering stem cell transplantation donor search even more complex in the future.
The presence of genomic imbalances is associated with poor outcome in patients with Burkitt Lymphoma treated with dose-intensive chemotherapy including rituximab

*Forero-Castro M (2016), British Journal of Haematology* [Link to abstract]

This study aimed to identify genomic changes that could predict treatment-response to chemotherapy and rituximab for Burkitt lymphoma. Forty Burkitt lymphoma patients were analyzed using array-based comparative genomic hybridization, and TP53, TCF3, ID3 and GNA13 mutations were assessed by next generation sequencing. Losses of 11q, 13q, 15q or 17p were associated with poor response to rituximab treatment, shortened PFS and OS. TP53 alterations were associated with shorter PFS and TCF3 alterations were associated with shorter OS.

- Genetic studies could potentially be used for risk stratification of Burkitt lymphoma patients.

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**Prognostic value of rare IKZF1 deletion in childhood B-cell precursor acute lymphoblastic leukemia: an international collaborative study**

*Boer, J (2016) Leukemia* [Link to abstract]

IKZF1 deletions in B precursor ALL is linked to unfavorable outcome, with high frequency in Ph+ and Ph-like ALL. The common deletion types DEL 4-7 and DEL 1-8 have proven prognostic value as single lesions. This is a case control study that looked at other rare variants of IKZF1 deletions to clarify their prognostic role. The study included patients from 9 international study groups, with a total of 134 rare IKZF1 variants and 402 matched controls. Poor EFS was shown in the matched pair analysis in all variant types.

- IKZF1-deletions (including both common and rare variants) may have a role as marker for risk stratification in ALL treatment protocols.

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**Second Cancer Risk Up to 40 Years after Treatment for Hodgkin’s Lymphoma**

*Schaapveld, M (2015), NEJM* [Link to abstract]

The authors report the relative risk of second cancer after treatment for Hodgkin Lymphoma (HL) to be significantly higher than in the general population, particularly for solid tumors. The standardized incidence ratio (SIR) was 4.6 in the study cohort as compared with the general population and remained elevated 35 years after treatment completion. Even though treatment toxicity was reduced over the last decades, the risk of a second malignancy remains largely unchanged. Results showed a small reduction in hematologic malignancies.

- The risk of second solid cancers did not change within the last 20 years despite reduction of toxicity and more restricted radiation fields.
NUDT15 c.415C>T increases risk of 6-mercaptopurine induced myelosuppression during maintenance therapy in children with acute lymphoblastic leukemia

Kanhatai Chiengthong (2016) Haematologica (Link to abstract)

This manuscript reports the effect of single nucleotide polymorphisms in ITPA and NUDT15 in a cohort of 82 pediatric ALL patients from Thailand. ITPA polymorphisms showed no difference in 6MP induced myelosuppression, and no difference in cumulative 6MP doses. Of the NUDT15 c.415 polymorphisms, 70 (85.4%), 10(12.2%), and 2 (2.4%) patients were CC, CT, and TT, respectively. NUDT15 c.415C>T was strongly associated with 6-MP induced early myelosuppression. Adjustment of 6MP doses according to blood counts resulted in lower median cumulative doses in NUDT15 c.415 CT and TT of 45% and 80%, respectively, compared to CC genotype. These results are consistent with results from Korean and Japanese studies (Yang, JCO 2015).

Dose adjustments of 6MP in ALL treatment based on polymorphisms in TPMT gene is well established. However, these TPMT variants are infrequent in most Asian populations and this article contributes to the understanding of NUDT15 polymorphisms in adjusting 6MP in Asian ethnicities.

Antilymphocyte Globulin for Prevention of Chronic Graft-versus-Host Disease

Nicolaus Kröger (2016), NEJM Link to abstract

This is a prospective, multicenter, open-label, randomized phase III study with analysis of the use of ATG as part of the myeloablative conditioning regimen for adults with leukemia undergoing allogeneic peripheral-blood HLA-identical sibling stem cell transplant. After 2 years, the cumulative incidence of chronic GVHD was 32.2% in the ATG group and 68.7% in the non-ATG group. Survival rate was similar but the composite end point of chronic GvHD-free survival and relapse-free survival was higher with ATG.

ATG was effective to prevent chronic GVHD in transplant when using peripheral blood stem cell source in matched sibling stem cell transplants without increasing OS.
Post transplant cyclophosphamide (PTC) has been shown to successfully modulate GVHD in preclinical models and in the adult population, enabling the patients to be completely off immune suppression on day +5. In this study, 11 pediatric patients were followed prospectively and received PTC for GVHD prophylaxis; they were compared to a retrospectively analyzed control group of 18 patients who received the standard therapy with calcineurin inhibitors. No acute nor chronic GVHD were seen in the PTC group, overall survival and event free survival were similar between the groups, and no significant difference was found with respect to relapse.

This is the first study in pediatric patients for treatment with single agent post transplant cyclophosphamide for GVHD prophylaxis after matched related SCT for hematological malignancies, showing promising results on a small group of patients that warrant further study.

Relapsed childhood acute lymphoblastic leukemia in the Nordic countries: prognostic factors, treatment and outcome

Trausti Oskarsson, (2016), Haematologica (Link to abstract)

This is an analysis of 516 patients with relapsed ALL report based on the cohort of the Nordic Society of Paediatric Haematology and Oncology (NOPHO) treated with the ALL-92 and ALL-2000 protocols, with total of 516 patients with relapsed ALL. Statistically significant adverse prognostic factors included shorter time to relapse (worse if earlier), site of relapse (worse if bone marrow involvement at relapse involving the bone marrow), age ten years or over at primary diagnosis, unfavorable cytogenetics, Down syndrome, and T-cell lineage with hyperleukocytosis at primary diagnosis. In the whole study population of relapsed ALL patients, the 5-year EFS was 43.7±2.3% and the 5-year OS was 51.5±2.3%. Further subgroup analysis based on time period, risk groups, relapse treatment protocols and HSCT are reported. Analysis of prognostic factors, validation of the current risk stratification and comparison of treatment modalities could be helpful in improving treatment for relapsed childhood ALL.

Outcomes of relapse ALL in a large population based cohort with long follow up period is presented in this paper. OS of this large cohort of relapsed pediatric ALL patients treated on the NOPHO ALL-92 and ALL-2000 was about 50% with confirmation of known adverse risk factors such as older age at diagnosis, unfavorable cytogenetics, T-cell lineage with hyperleukocytosis, Down syndrome, shorter time to relapse, and bone marrow involvement at relapse.
Review: A risk-adapted approach to acute GVHD to treatment: are we there yet?

Holtan, SG et al (2016) BMT, (Link to abstract)

Only approximately 50% of patients have steroid-responsive aGVHD. Pre-HSCT co-morbidity is a critical factor in both probability of developing aGVHD and mortality after it. Current risk-stratification models do not take into account endothelial factors, including VEGF and thrombomodulin production, and gut microbiota, all of which influence healing and potential for steroid-responsiveness. A refined Minnesota risk score based on severity of symptoms and number of organ systems involved was recently published. Serum biomarkers including TNFR1, REG3α, and ST2 may also be incorporated in the future.

Risk stratification for aGVHD is improving but is not yet able to prognosticate with certainty or help dictate treatment.

REVIEWS/ PERSPECTIVES

Revisiting the biology of infant t(4;11)/MLL-AF4+ B-cell acute lymphoblastic leukemia

Sanjuan-Pla A, 2015, Blood (Link to abstract)

Molecular landscape of acute myeloid leukemia in younger adults and its clinical relevance

Grimwalde D, 2016, Blood (Link to abstract)

Epigenetics and approaches to targeted epigenetic therapy in acute myeloid leukemia

Wouters BJ, 2016, Blood (Link to abstract)

Emerging therapeutic drugs for AML

Stein EM, 2016, Blood (Link to abstract)

Pediatric chronic myeloid leukemia is a unique disease that requires a different approach

Hijiya N, 2016, Blood (Link to abstract)
Germline Mutations in Predisposition Genes in Pediatric Cancer

Jinghui Zhang, (2015), NEJM Link to abstract:

The authors performed whole-genome, whole-exome, or both types of sequencing on germline DNA in 1120 pediatric cancer patients younger than 20 years of age in order to identify the prevalence of predisposing mutations. The cohort represented a wide array of the most common childhood cancers of hematologic and solid nature. 8.5% of the patients with cancer had a mutation that was considered to be pathogenic or probably pathogenic. Common mutated genes were TP53, APC, BRCA2, NF1, PMS2, RB1 and RUNX1.

- Current methods identify about 8.5% of pediatric patients to harbor a pathogenic or probably pathogenic cancer-predisposing mutation in their germline DNA.

Mutations in the transcriptional repressor REST predispose to Wilms tumor.

Mahamdallie, S (2015) Nature Genetics (Link to abstract)

Analysis of whole exome sequencing data of familial Wilms tumor samples revealed several pathogenic mutations in the REST gene (encoding RE1-silencing transcription factor). The authors further analyzed (presumably) non-familial WT and found pathogenic mutations in a small percentage of patients. All 11 different mutations clustered in the DNA-binding domain of REST.

- REST mutations account for 2% of WT, similar to germline WT1. The authors suggest that screening for REST mutations in familial WT would be prudent and facilitate surveillance of relatives.

Identification of Novel Fusion Genes in Testicular Germ Cell Tumors

Hoff, AM, (2016) Cancer Research (Link to abstract)

Testicular GCTs are mutationally quiet other than frequent gain at 12p but had not yet been comprehensively examined for gene fusions. Next generation RNA sequencing is now the best available technology for detecting fusions not visible through standard techniques such as FISH or RT-PCR. The group examined embryonal carcinoma cell lines as well as 24 testicular GCTs with different histologic subtypes. They found 8 previously undescribed fusion transcripts commonly involving the RCC1 gene or internal translocations of ETV6.

- This study reveals that testicular GCTs are more marked by fusions than by mutations similar to childhood sarcomas.
TERT rearrangements are frequent in neuroblastoma and identify aggressive tumors.

Valentijn, L (2015), Nature Genetics (Link to abstract)

Whole-genome sequencing of 75 high-risk neuroblastoma tumor samples detected structural rearrangements and overexpression of TERT in 23%. This is the second most common alteration in HR-neuroblastomas after MYCN and associated with poor prognosis. TERT rearrangements, MYCN amplifications and ATRX deletions define 3 distinct, non-overlapping subgroups of high-risk neuroblastoma.

Another paper in a series of recent studies showing that telomerase activation is common in high-risk neuroblastoma, mutually exclusive with ATRX deletion and MYCN amplification and associated with poor outcome.

Tandem high-dose chemotherapy with thiotepa and busulfan-melphalan and autologous stem cell transplantation in very high-risk neuroblastoma patients.

Pasqualini, C 2016, BMT (Link to abstract)

This is an European study (2004-2011) of very high risk (VHR) NBL patients (HR patients who had metastatic disease at end of induction) had therapy intensified to received two tandem autologous HSCTs with thiotepa, then busulfan-melphalan, with a two-month interval between. Defibrotide VOD prophylaxis was standard practice. 26 patients received tandem transplants and only 5 were MYCN amplified. Six patients (25%) developed VOD, one died, toxicity was otherwise typical of autologous HSCT, but higher rate and severity with the second transplant. 6/24 patients achieved CR, 7 PR, 10 stable disease. OS at 3 years was 69%, EFS was 37.3%.

[*In comparison, following ANBL0532 HR NB study, COG recommends the use of tandem transplant consolidation (with thiotepa/cyclophosphamide then carbo, etop, melphalan (CEM)) for patients greater than 18 months of age with INSS stage 4 neuroblastoma or those of any age with INSS stage 2B, 3 or 4 and MYCN amplification high-risk neuroblastoma based upon the significantly improved 3-year EFS following tandem transplant.*]

The outcome in this cohort was promising and it appeared to be safe to perform tandem transplant with VHR NBL. An upcoming SIOPEN study will compare tandem HDC with thiotepa and BuMEL (this protocol) with mIBG/BuMel autoHSCT.
Section 4. Supportive Care, Survivorship, General Pediatrics & other updates

Neurodevelopmental Outcome at 2 Years of Age After General Anaesthesia and Awake-Regional Anaesthesia in Infancy (GAS): an International Multicentre, Randomized Controlled Trial


This paper reports the secondary outcome of an RCT comparing neurodevelopmental outcomes in infants undergoing surgery for inguinal hernias. The randomization is between general anaesthesia (sevofluorane) and regional awake anaesthesia. The outcome reported here is neurodevelopmental outcome at 2 years of age by the Bayley scale. 360 infants less than 60 weeks postmenstrual age (premature babies were included) were in each arm in the intention to treat analysis although 69 in the regional group were converted to general anaesthesia. There was no difference in the mean of the composite cognitive score between the groups. The analysis reported here was a per-protocol analysis (not intention to treat).

This is a hot area of contention in all fields of paediatrics – how much harm are we doing to our young patients when we put them under GA? This RCT (the first to ask this question) suggests the harm may not be real. But bear in mind that these children underwent a single short procedure – not multiple GAs over the course of the year the way our patients do. The primary outcome is the Weschler intelligence scale at 5 years of age and will be reported in the future.

REVIEW/ PERSPECTIVES

Preclinical Models Provide Scientific Justification and Translational Relevance for Moving Novel Therapeutics into Clinical Trials for Pediatric Cancer

Langenau, DM, 2015, Cancer Research (Link to abstract)

Essential Components of Cancer Education

Welch, DR, 2015, Cancer Research (Link to abstract)