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ABSTRACT

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QUALITY MANAGEMENT GROUP—ORAL SESSION

O169
Cost-Effectiveness of Axicabtagene Ciloleucel for Adult Patients with Relapsed or Refractory Large B-Cell Lymphoma in the United States

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Background: Axicabtagene ciloleucel (axi-cel) is a CD19-directed chimeric antigen receptor (CAR) T-cell therapy which has been approved by the U.S. Food and Drug Administration. The pivotal study ZUMA-1 demonstrated an objective response rate of 82%, and the median overall survival (OS) has not been reached after at least 12 months of follow-up (Neelapu et al. 2017). To better understand the economic implications of axi-cel, we developed a decision model to estimate the cost-effectiveness of axi-cel compared to salvage chemotherapy from a U.S. payer perspective.

Methods: A partitioned survival model was developed to assess the overall costs and outcomes of axi-cel compared to salvage chemotherapy. We modeled the treatment choices with a decision-tree framework and then use a long-term Markov structure to assess progression-free and progressed disease health states. We modeled the axi-cel arm based on the one year follow-up updated analysis of ZUMA-1 (Neelapu et al. 2017) and the salvage chemotherapy arm using the SCHOLAR-1 study (Crump et al. 2017). We used the observed Kaplan-Meier curves for OS and progression free survival (PFS) from both studies. Mixture cure modelling (Othus et al. 2017) was applied to estimate the proportion of patients with long-term remissions. Health utility data was based on published literature (Chen et al. 2017). The U.S. list price ($373,000) of axi-cel was used. We used patient-level data (ZUMA-1), literature, guidelines and expert opinion to inform the health resource utilization for pre-treatment (pre-conditioning chemotherapy, apheresis) and treatments (axi-cel or R-DHAP, hospitalization, adverse event, subsequent stem cell transplantation). Unit costs were from U.S. wholesale acquisition costs and Medicare reimbursement schedules. Uncertainty analysis included one-way and probabilistic sensitivity analyses of all model inputs. Life years (LYs), quality-adjusted life years (QALYs), and costs were generated over a lifetime, with discount rate at 3% per year in the base case.

Results: In the base case, total LYs, QALYs, and costs were 9.5, 7.9, and $454,222 for the axi-cel treatment vs. 2.6, 2.2, and $132,038 for the salvage chemotherapy treatment. The corresponding axi-cel cost per QALY gained was $56,114. In one-way sensitivity analysis, the cost-effectiveness of axi-cel was most sensitive to 1) the proportion with axi-cel long-term remission, 2) the discount rate, 3) the axi-cel price. Probabilistic sensitivity analysis showed 96% and >99% likelihood of axi-cel being cost-effective at a societal willingness to pay thresholds of $100,000 and $150,000 per QALY.

Conclusions: Axi-cel may be a cost-effective alternative to salvage chemotherapy for adults with R/R-LBCL in the U.S. Since follow-up data are limited for patients treated with axi-cel, continued evaluation of outcomes and costs are necessary to better understand the value of this novel therapy over years of patient experience.

Conflict of interest: J. Roth, S. Sullivan, and S. Ramsey are consultants for this research.

V. Lin, A. Purdum, L. Navale, and P. Cheng are employees and equity owners of Kite, a Gilead Company

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O170
ROME TRANSPLANT NETWORK, A MODEL OF JACIE ACCREDITED METROPOLITAN HEMATOPOIETIC STEM CELL TRANSPLANT PROGRAM

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Background: Rome Transplant Network (RTN) is a JACIE accredited Metropolitan Hematopoietic Stem Cell Transplant Program established in Rome from 2006 as a cooperative network among 6 Transplant Centers for a total of 10 Clinical, Cell Collection and Cell Processing Units with the collaboration of 2 further JACIE accredited Cell Processing Units (Bambino Gesù Hospital, St. Camillo-Forlanini Hospital). RTN is registred at EBMT with the unique CIC 756. The RTN includes one single Director of the Transplant Program and a Principle Responsible for each Units.

Objectives of RTN are **1)** to standardize transplant procedures for each line of autologous or allogeneic transplant program; **2**) to improve quality of transplant care; **3)** to extend the potential of transplant activity over the metropolitan area; **4**) to share expertise and professional education among healthcare providers; **5**) to promote excellence of single transplant Centers; **6**) to rationalize cost-management of public health. RTN is an innovative entity, which follows rules and standards established by JACIE accreditation program.

Methods: The RTN is structured on 3 levels: **1) first level:** the Director responsible for coordinating the whole Transplant Program and the headed staff represented by the Quality Management and the Data Managing Offices. **2) second level:** the Boards including Clinical and Laboratory Directors of each clinical, cell collection and cell manipulation Units and representative heads of nursing staff. The Boards are in charge of approving documents and quality assurance related to each facility, of sharing and developing clinical protocols and of evaluating personnel and its continuous training. **3) third level:** medical, biological and nursing individuals involved in the Clinical, Cell Collection and Cell Manipulation Units. Documental System. The RTN documental system reflects the complexity of the organization. There are 2 categories of documents: **a)** newly developed documents edited by the Boards and **b)** already existing documents within the single Centers to be endorsed by the RTN and hence, validated by the Boards. A **Quality Plan** for every Board (clinical, collection, manipulation, nursing) and a Quality Plan for the whole transplant program have been produced. **Computer Platforms** play an extremely important role for either the rationalization of activities or the management of information, sharing know-how and communication among the RTN operators. In particular, 2 computer tools have been implemented: one for the management of cell products in all stages of the process: collection, manipulation, storage and infusion and the other one sharing and spreading documentation among all the RTN Units, managing the common database of transplant patients and monitoring all clinical studies.

Results: In the last 10 years, the RTN transplant activity progressively increased from 138 transplants in 2006 to 200 transplants registered in 2016 for a total of 1803 transplants.

Conclusions: RTN represents a major innovation in the organization of transplant activity aimed at improving the single center excellence and the quality level of public health.

Conflict of interest: No conflict of interest

O171
Use of a Patient-Reported Physical Function Measure Allows Clinically-Pragmatic, Individually-Tailored Exercise Interventions for People with Chronic Graft-Versus-Host Disease

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Background: Best practice guidelines for the care of people with cGVHD require measurement, tracking, and intervention to improve patient physical function, but wide adoption of exercise interventions has not occurred due to a lack of clinically-pragmatic exercise implementations, and particularly due to the absence of useful functional status metrics for this population.

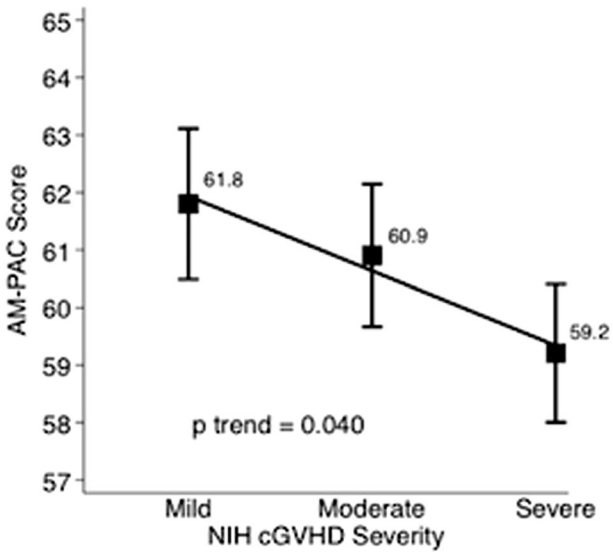
Methods: The Activity Measure for Post-Acute Care™ outpatient basic mobility short form (AM-PAC) is an 18-item patient- or clinician-reported questionnaire, designed to assess functional mobility in outpatient clinical settings. In this project, the AM-PAC was used by a clinically-integrated physical therapist (CI-PT) to stage patients by self-reported mobility level. For example, a person with AM-PAC stage 3 has unlimited functional mobility within the home, but has difficulty with functional mobility outside of the home. Similarly, a person with AM-PAC stage 2 has difficulty with functional mobility inside the home, and a person with AM-PAC stage 1 has difficulty with functional bed mobility. Exercise interventions by the CI-PT were tailored to the AM-PAC stage, and included a home exercise prescription with modifications made at regular clinic visits. For analysis, patient data was grouped by provider-reported NIH Severity Score for cGVHD (NIHSS) values, and adjusted mean AM-PAC scores were calculated for each NIHSS group. Logistic regression was performed to assess differences in functional mobility between people with no or mild cGVHD (NIHSS = 0 or 1), and people with moderate or severe cGVHD (NIHSS = 2 or 3). All analyses were adjusted for patient age, sex, and comorbidity level, represented by Charlson Comorbidity Index value.

Results: 955 AM-PAC and NIHSS scores were collected between November 2016 and August 2017, from 203 unique people with cGVHD after allogeneic stem cell transplant. Overall, 63.4% of AM-PAC scores were in stages 1–3, indicating that the bulk of patients had functional limitations due to impaired mobility. Adjusted mean AM-PAC values for patients with NIHSS 1, 2, and 3 were 61.9 (95%CI 59.6, 64.4), 61.3 (95%CI 58.7, 62.6), and 59.7 (95%CI 56.9, 61.6) respectively (see figure 1).

All adjusted mean AM-PAC values were in AM-PAC stage 3, demonstrating the ubiquity of functional loss. Logistic regression showed that people with moderate or severe cGVHD (NIHSS = 2 or 3) had significantly worse functional mobility (AMPAC stage 1,2,3) than people with no or mild cGVHD (NIHSS = 0 or 1) (Chi-squared statistic = 24.2, $p < .001$).

Conclusions: Patient-reported functional mobility status, assessed by AM-PAC score, was significantly lower among people with higher cGVHD severity. Though functional mobility limitations were common for all people with cGVHD, there was a significant trend of increased functional loss for people with more severe cGVHD. This indicates that the AM-PAC may be a useful metric to describe and monitor physical function for people with cGVHD. In this project, a CI-PT used AM-PAC mobility stage to prescribe and manage a pragmatic exercise intervention. This innovative approach was made possible through the use of a lightweight, meaningful measure of patient physical function, an approach that has real potential to overcome the barriers to implementation of exercise for people with cGVHD.

Conflict of interest: None of the authors has anything to disclose.



O172
Monitoring defibrotide usage in paediatric patients undergoing HSCT with known risk factors for developing VOD/ SOS

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Background: Defibrotide is licensed for the treatment of hepatic venous occlusive disease (VOD) following haematopoeitic stem cell transplant (HSCT). VOD is characterized by endothelial injury and non-thrombotic obstruction of small intra-hepatic venules that may lead

to liver damage. Up to April 2015 defibrotide was used as prophylaxis against VOD in our HSCT patients who were considered at high-risk for developing VOD. This practice was discontinued due to the lack of evidence of efficacy and increasing costs of the drug. The aims of this audit were to identify patients undergoing HSCT who had one or more risk factors for the development of VOD, to measure the incidence of VOD in this patient cohort after the discontinuation of prophylactic defibrotide and calculate the cost savings associated with the discontinuation of prophylaxis

Methods: All patients who underwent HSCT in Our Lady's Children's Hospital between Oct 2015 and Dec 2016 were included. All patient's medical records were reviewed and risk factors for VOD were identified. The risk factors for developing VOD post HSCT in our patient cohort were defined following a literature review of peer-reviewed papers identifying paediatric specific risk factors and the listed risk factors in the EBMT 2012 handbook. These were namely: patients aged ≤ 2 years, patients receiving a second transplant, conditioning with IV busulfan +/− cyclophosphamide, and previous treatment with gemtuzumab ozogamicin. The theoretical dose of defibrotide for patients with known risk factors was calculated based on their weight at start of conditioning and the duration of treatment was based on the number of days conditioning the patient received plus 30 days following the date of transplant. The cost of a theoretical course of defibrotide for these patients was calculated to determine cost savings.

Results: Of the 27 patients included in the audit, 16 (59%) had one or more risk factors, 6 (22%) of whom had two risk factors and one patient had three risk factors for developing VOD. The most common risk factor identified was conditioning with busulfan in patients ≤ 2 years of age (26% of patients). Three patients received conditioning with busulfan and cyclophosphamide and two of these patients were ≤ 2 years. Two patients ≤ 2years were not considered at risk as they received minimal conditioning. One patient received no conditioning chemotherapy and the second patient underwent an autologous HSCT with carboplatin and thiotepa conditioning treatment. At present no patient post HSCT has developed VOD requiring treatment. One patient developed subclinical VOD which required no treatment and resolved spontaneously. Another patient received defibrotide as prophylaxis for VOD due to severe liver dysfunction prior to HSCT. There were substantial cost savings following the discontinuation of prophylactic defibrotide with a total of 2876 vials (180 vials/ patient) saved during this time period.

Conclusions: This audit validates our decision to discontinue use of prophylactic defibrotide and reserve its use for treatment of early VOD.

Conflict of interest: None of the authors has anything to disclose.