less directly applicable to patient populations for NICE/SMC/AWMSG evaluations. The UK will either need to try and maintain harmonisation with the EU or create a more efficient and simpler regulatory process to ensure the UK remains a primary site to host CTs.

HT2

HEALTH TECHNOLOGY ASSESSMENT DECISIONS IN IMMUNO-ONCOLOGY THERAPIES: RESULTS, RATIONALES, AND TRENDS

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OBJECTIVES: Immuno-oncology (IO) therapies have emerged as a promising drug class in cancer treatment with targeted mechanisms of action. Some IO therapies have demonstrated durable clinical responses beyond conventional standards of care. As the IO landscape continues to expand, it becomes important to assess their value with regard to clinical benefit and costs. Health technology assessments (HTAs) aim to manage access and expense of new treatments to provide cost-effective treatment options. The objective of this analysis was to evaluate recent IO HTA decisions and their rationale to identify trends in selected countries. **METHODS:** HTA surveillance was conducted for Australia, Canada, France, Germany, and the United Kingdom (UK) from January 1, 2012 to April 30, 2017 (64 months). HTAs for IO therapies were evaluated by therapeutic area, decision, and rationale for each decision. Decisions were categorized as favorable, unfavorable, mixed (both favorable and unfavorable), or neutral (eg, deferred decision). **RESULTS:** 41 IO HTAs were published during the study timeframe: 23 (56%) in melanoma, 12 (29%) in non-small cell lung cancer, and 6 (15%) in renal cell carcinoma. Across HTAs examined, 26 (63%) decisions were favorable, 11 (27%) were unfavorable, 2 (5%) were mixed, and 2 (5%) were neutral. All decisions were deemed favorable in France (6/6, 100%) and the UK (8/8, 100%), followed by Canada (6/7, 86%), Germany (4/9, 44%), and Australia (2/11, 18%). Favorable decisions stemmed from strong evidence of clinical benefit and high unmet need, whereas unfavorable decisions were typically due to inappropriate comparators or unacceptable incremental cost-effectiveness ratios. Mixed and neutral decisions were heavily dependent on effectiveness in specific subpopulations, including patients previously treated, patients with specific gene mutations, or elderly patients. **CONCLUSIONS:** As new IO therapies emerge and attain additional indications, it is critical that HTA submissions provide strong clinical and pharmacoeconomic evidence to achieve access.

HT3

ANALYSIS OF FACTORS INFLUENCING THE LEVEL OF ACTUAL BENEFIT IN HEALTH TECHNOLOGY ASSESSMENT

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OBJECTIVES: The reimbursement level of drugs in France is based on their medical assessment by the Transparency Committee. The aim of this study is to understand the rationale behind the assessment of drugs in all therapeutic areas except oncology by determining the criteria that influence the Actual Benefit (AB) levels. **METHODS:** We performed a retrospective analysis between January 2014 and March 2017 of the new products and the new indications but oncology drugs were excluded. We searched relevant criteria of the Actual Benefit assessment carried out in each indication pertaining to the drug evaluation from the opinion of the Transparency Committee. **RESULTS:** In total, 88 drugs in 111 indications were evaluated including 43 moderate AB, 12 mild AB and 56 insufficient AB. Among the criteria taken into account in the AB, we found the following relations: a better clinical efficacy/effectiveness and safety ratio of the medicine led to a better AB (80% of the moderate benefit-risk ratio obtained a moderate AB, 50% of the low benefit-risk ratios obtained a mild AB and 100% insufficient benefit-risk ratio obtained an insufficient AB). Treatments of 3rd or last intention or that have no place in the therapeutic strategy led to mild and insufficient AB (95% of the cases). As to the methodology, most moderate AB was obtained with superiority comparative (88% of cases) and phase III (93% of cases) studies. A non-randomized and non-double-blind study leads to insufficient AB (except for an open case) and finally, we found that moderate AB could be obtained with placebo-controlled studies despite the presence of therapeutic alternatives (42% of cases). **CONCLUSIONS:** The factors influencing the moderate, mild and insufficient AB levels were the clinical efficacy/effectiveness and safety of the medicine, the therapeutic strategy as regards to therapeutic alternatives and the methodology of the study (randomization, blinding and kind of study).

HT4

USING REAL-WORLD DATA (RWD) IN HEALTH TECHNOLOGY ASSESSMENT (HTA) PRACTICE: A COMPARATIVE STUDY OF 5 HTA AGENCIES

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OBJECTIVES: Reimbursement decisions are conventionally based on evidence from randomised controlled trials (RCTs) which often have high internal validity but low external validity. Real-world data (RWD) may provide complimentary evidence for relative effectiveness assessments (REAs) and cost-effectiveness assessments (CEAs). This study examines whether RWD is incorporated in Health Technology Assessment (HTA) of melanoma drugs by European HTA agencies, differences in RWD use between agencies and across time. **METHODS:** HTA reports published between 01.01.2011 and 31.12.2016 were retrieved from websites of agencies representing 5 jurisdictions: England (NICE), Scotland (SMC), France (HAS), Germany (IQWiG) and the Netherlands (ZIN). A standardized data-extraction form was used to extract information on RWD inclusion for both REAs and CEAs. A panel of senior HTA assessors representing the 5 agencies was consulted to check the robustness of data extracted and interpretation. **RESULTS:** Fifty-two reports were retrieved. All 52 reports contained REAs; CEAs were present in 25. RWD was included in 28 of 52 REAs (54%); mainly to estimate melanoma prevalence. RWD was included in 22 of 25 (88%) of CEAs; mainly to extrapolate long-term effectiveness and/or identify drug-related costs drugs. Differences emerged between agencies regarding RWD use in REAs; ZIN and IQWiG cited RWD for evidence on prevalence whereas NICE, SMC and HAS additionally cited RWD use for drug effectiveness. No visible trend for RWD use in REAs and CEAs over time was observed. **CONCLUSIONS:** In general, RWD inclusion was higher in CEAs than REAs. It was mostly used to estimate melanoma prevalence in REAs or to predict long-term effectiveness in CEAs. Differences emerged between agencies' use of RWD. However, no visible trends for RWD use over time were observed. Future research should explore the use of RWD in HTA of drugs in other disease indications and in conditional reimbursement schemes.

BREAKOUT SESSION IV

P4: RESEARCH ON METHODS

RM1

NETWORK META-ANALYSIS OF HAZARD RATIOS VS. FRACTIONAL POLYNOMIALS APPROACH IN A COST-EFFECTIVENESS ANALYSIS CONSIDERING ADVANCED GASTRIC CANCER

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OBJECTIVES: Network meta-analysis (NMA) is a valuable tool for evidence synthesis, which estimates relative treatment effects between comparators in the absence of head-to-head data, and often in the form of a hazard ratio (HR). Utilising HRs relies on the proportional hazards (PH) assumption which is often shown to be violated and can have a substantial impact on survival outcomes and thus cost-effectiveness results. A more flexible and informative approach such as an NMA using fractional polynomials could be considered which incorporates additional parameters associated with the treatment effect and does not rely on the PH assumption. Our objective is to explore the difference in outcomes within a cost-effectiveness analysis using traditional NMA methods compared with a more sophisticated fractional polynomial approach to evidence synthesis for advanced gastric cancer (AGC). **METHODS:** A cost-effectiveness model was built considering the treatment of AGC. The model implemented a Markov structure considering a UK National Health Service perspective. The model sourced efficacy data from both fractional polynomial analyses presented in Harvey (2017) and a conventional NMA conducted on these data. HRs obtained from the NMA were applied to pooled data for best supportive care (BSC). Health-related quality of life data were obtained from the literature and costs were sourced from UK-specific references (2015-16 cost year). **RESULTS:** Results show that estimating efficacy using fractional polynomials consistently reduced the survival benefit for treatments vs. BSC compared with the traditional NMA approach, ceteris paribus. This trend was observed in all scenarios with reductions estimated up to 52.45%. A reduction in the survival benefit increased estimates of incremental cost-effectiveness for all comparators vs. BSC. **CONCLUSIONS:** When the PH assumption does not hold, traditional methods of synthesis may result in biased comparative efficacy estimates which impact important decisions of cost-effectiveness. The extent of this bias will vary based on the data available.

RM2

MULTIVARIATE NETWORK META-ANALYSIS OF SURVIVAL FUNCTION PARAMETERS

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OBJECTIVES: Recently, network meta-analysis of survival data with a multi-dimensional treatment effect was introduced using fractional polynomial (FP) distribution. With these models, the hazard ratio is not assumed to be constant over time, thereby reducing the possibility of violating consistency in indirect comparisons. However, beyond the FP models it is challenging to assess parametric distributions often used for cost-effectiveness models in health technology assessments (HTA). We aim to develop a two-step network meta-analysis (NMA) for time-to-event data. **METHODS:** First, for each arm of every randomized controlled trial (RCT) connected in the network of evidence simulated patient data were fit to alternative parametric distributions, including exponential, Weibull, Gompertz, log-normal, log logistic, gamma, and generalized gamma. For each distribution, the resulting scale and shape parameters per arm were then included in a multivariate NMA, which preserved randomization and accounted for the correlation between the parameters. Results were compared to FP models to validate results and evaluate any differences. **RESULTS:** An illustrative analysis is presented for a network of RCTs evaluating interventions for advanced melanoma. The NMA was assessed using alternative distributions, which were compared using Akaike information criterion, which would facilitate model averaging to propagate structural uncertainty in a cost-effectiveness analysis. Based on the generalized gamma distribution, the difference in mu, Q, and sigma parameters for each treatment versus dacarbazine (DTIC) were: Non-DTIC: 0.41 (-0.19,1.01), 0.12 (-0.08,0.32), 0.39 (-0.7,1.49); DTIC+ Interferon (IFN): 0.24 (-0.15,0.69), -0.07 (-0.24,0.11), 0.45 (-0.87,1.66); DTIC+non-IFN: 0.22 (-0.13,0.65), -0.05 (-0.21,0.11), -0.17 (-1.13,1.1). **CONCLUSIONS:** A two-step NMA of survival data allows for a straightforward comparison of alternative parametric distributions in terms of goodness of fit by avoiding the need to specify each distribution in WinBUGS. This approach provides a more generalizable evidence synthesis framework for HTA.