and overseas databases including Ovid-MEDLINE, Ovid-EMBASE and Cochrane Library. Total of 274 studies were searched and 6 studies were included in the final assessment. Each of the stages from literature search and extraction of data were carried out independently by 2 researchers. **RESULTS:** The effectiveness of CBL gene mutation test was assessed by CBL gene mutation detection rate, relevance between CBL gene mutation and clinical symptoms, and impact on medical decisions. The CBL gene mutation detection rate was 5 to 19% among JMML patients. The hemoglobin level and age-at-diagnosis were both significantly low among patients with a CBL gene mutation (p=.02, p=.037). There was intent to assess the impact of detecting CBL gene mutation on the medical decisions such as changes in the treatment plan and/or method; however, there were no studies reporting on this matter. **CONCLUSIONS:** There is a need for quick and accurate diagnosis for JMML, which is an intractable disease occurring in childhood, and the test in question can be helpful in deciding on stem cell transplantation. Also, considering that CBL gene mutation occurs exclusively from other gene mutations (PTPN11, RAS, NF1, etc.) causing JMML, it was deemed that even a low detection rate of 5 to 19% had a clinical significance. The CBL gene mutation test is an effective test that can contribute to the diagnosis of JMML and help determine the treatment strategy (Grade of recommendation: C).

PND8

CONFIRMED DISABILITY IMPROVEMENT IN PATIENTS WITH ACTIVE MULTIPLE SCLEROSIS TREATED WITH FINGOLIMOD VERSUS BRACE: A MATCHED COMPARISON OF TREATMENTS FROM THE PANGAEA AND PEARL REGISTRY STUDIES

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OBJECTIVES: To compare confirmed disability improvement in propensity score (PS)-matched cohorts of patients receiving fingolimod or BRACE (beta-interferons or glatiramer acetate) following previous BRACE treatment, who had active multiple sclerosis (MS), using data from two German observational studies, PANGAEA and PEARL, respectively. **METHODS:** Patients with active MS (≥1 relapse in the year before the study) from the PANGAEA and PEARL registries were included if they had received BRACE before participating in the studies and did not have missing relapse data in the previous year. Patients from the PANGAEA registry were excluded if they had participated in PEARL. Patients in the PANGAEA cohort were matched in a 3:1 ratio to patients in the PEARL cohort using a PS-matching approach. Time to 3-month and 6-month confirmed disability improvement was assessed using a Kaplan–Meier approach. Hazard ratios for confirmed disability improvement (fingolimod vs BRACE) were estimated using a Cox proportional hazards model. **RESULTS:** After PS matching, a total of 1535 patients were included (PANGAEA, n=1163; PEARL, n=372). The proportions of patients in the PANGAEA and PEARL cohorts with 3-month confirmed disability improvement were 14.6% and 7.0%, respectively (p<0.001). Similar results were seen for 6-month confirmed disability improvement (11.0% vs 6.2%; p<0.001). The probability of 3-month confirmed disability improvement was significantly higher in PANGAEA compared with PEARL (175% increase; HR, 2.75; 95% CI, 1.82–4.15; p<0.001). The corresponding value for 6-month confirmed disability improvement was a 126% increase (2.26; 1.45–3.53; p<0.001). Similar findings were found in subgroups of patients with at least 1 year of follow-up (3-month: 176% increase; 2.76, 1.80–4.22; p<0.001; 6-month: 136% increase; 2.36, 1.50–3.69; p<0.001). **CONCLUSIONS:** This comparison of real-world cohorts of patients with MS demonstrates that fingolimod treatment is associated with statistically significant increases in the probability of confirmed disability improvement compared with BRACE.

PND9

ADJUSTED INDIRECT COMPARISON OF ORAL MULTIPLE SCLEROSIS AGENTS

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OBJECTIVES: BG-12 and Teriflunomide are the first two oral therapeutics for the treatment of Multiple Sclerosis. At the moment there is no direct comparison of these agents. The adjusted indirect comparison is a comparison of different therapies adjusted according to their direct comparison results against a common control, so that the strength of the randomised trials is preserved. **METHODS:** A Systematic literature search was conducted in the databases of Medline, Embase and Cochrane. Due to a lack of direct evidence an adjusted indirect comparison by Bucher in efficacy endpoints was performed. The risk of bias tool was used to assess the methodological quality of the included studies. **RESULTS:** 339 studies were identified in a systematic literature search. Finally four RCTs were eligible in which 4861 patients had been randomized. All included studies have a low risk of bias. There were no significant heterogeneity between the included studies in the operationalization of the relevant endpoints for AIC. Adjusted Indirect comparisons could be performed in the endpoints annual relapse rate, percentage of relapse free patients and percentage of patients with EDSS progression. In the annualized relapse rate BG-12 gains a statistically significant 44% risk reduction against Laquinimod (RR=0,66 [0,52;0,85]) and 26% against Teriflunomide (RR=0,74 [0,56;0,99). In no other endpoint the results were significant. **CONCLUSIONS:** It can be assumed that the relapse risk under BG-12 is less than under Laquinimod or Teriflunomide. The possible superiority of BG-12 has to be checked with the help of further direct comparative RCTs.

PND10

COMPARATIVE EFFECTIVENESS USING A MATCHING-ADJUSTED INDIRECT COMPARISON BETWEEN DELAYED-RELEASE DIMETHYL FUMARATE AND FINGOLIMOD FOR THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS

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OBJECTIVES: Delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF) and fingolimod are oral disease-modifying treatments for relapsing-remitting multiple sclerosis (RRMS). Direct comparisons of these agents are not possible due to a lack of head-to-head trials. In this study, comparative effectiveness research was conducted by indirectly comparing efficacy outcomes at 2 years with DMF or fingolimod treatment of RRMS in Phase 3 studies. **METHODS:** Individual patient data from the DEFINE and CONFIRM studies of DMF (pooled) and aggregate data from the FREEDOMS and FREEDOMS II studies of fingolimod (pooled using random effects meta-analysis) were utilised. Only results using the approved dosage of DMF (240 mg twice daily) and fingolimod (0.5 mg once daily) are reported. Matching-adjusted indirect comparison was conducted as described in Signorovitch et al (2010). Patients in the pooled DMF trials were weighted such that their average baseline characteristics (age, gender, time from onset of symptoms, Expanded Disability Status Scale score, number of relapses in previous year) matched those reported for patients in pooled fingolimod trials. After matching, weighted efficacy outcomes for patients treated with DMF were compared with summary efficacy outcomes for patients treated with fingolimod. **RESULTS:** After matching, all baseline characteristics were balanced between the pooled DMF trials and the pooled fingolimod trials. At 2 years, annualised relapse rate ratio (95% confidence interval [CI]) for DMF vs placebo was 0.52 (0.43, 0.62) and for fingolimod vs placebo was 0.48 (0.42, 0.55). Twelve-week confirmed disease progression hazard ratio (95% CI) for DMF vs placebo was 0.70 (0.57, 0.85) and for fingolimod vs placebo was 0.76 (0.61, 0.95). Additional data, including comparison of DMF vs fingolimod, will be presented. **CONCLUSIONS:** In a matching-adjusted indirect comparison, the efficacy of DMF was similar to that of fingolimod on clinical measures of relapse and disability progression.

PND11

RANKING OF DISEASE-MODIFYING THERAPIES FOR MULTIPLE SCLEROSIS

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OBJECTIVES: Relapses and disability progression are the clinical hallmarks of MS and the two most commonly assessed endpoints for therapeutic interventions in clinical trials. For many patients relapses are the initial defining feature of MS. However, the accumulation of disability has the greatest long-term clinical, social and economic impact on patients and society. This study evaluated the comparative efficacy of disease-modifying therapies for multiple sclerosis and ranked each therapy based on probabilities of being among the best treatments for each outcome. **METHODS:** A network meta-analysis was conducted within a Bayesian framework to estimate comparative annualised relapse rates (ARR) and risks of disability progression (defined by both a 3-month, and 6-month confirmation interval). Cumulative ranking analysis, using the Surface Under the Cumulative RAnking curve (SUCRA) method, provided a ranking of treatments for each outcome. **RESULTS:** Alemtuzumab and natalizumab had the highest SUCRA scores for ARR (>90%) and disability progression confirmed after three months (>80%), while IFN β-1a 30mcg ranked lowest among active treatments for these outcomes. Ranking of treatments was affected by the definition of disability progression largely due to the conflicting results of IFN β-1b 250 mcg, ranking among the most efficacious treatments for disability progression confirmed after six months (>90%) and among the least efficacious for disability progression confirmed after three months (<50%). Alemtuzumab and natalizumab both scored relatively highly for disability progression confirmed after six months. Notable variation in ranking across outcomes was observed for fingolimod (>70% for ARR, <50% for the disability progression outcomes). **CONCLUSIONS:** The magnitude of treatment effects and associated uncertainty varied between DMTs, and across outcomes. While natalizumab and alemtuzumab demonstrated consistently high ranking for both relapse and progression, with older interferon-beta and glatiramer acetate products ranking lowest, variation in disability progression definitions lead to variation in the relative ranking of treatments.

PND13

EPIDEMIOLOGY AND CURRENT TREATMENT OF NEUROMYELITIS OPTICA: A SYSTEMATIC REVIEW

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OBJECTIVES: Neuromyelitis Optica (NMO) has been described as a disease clinically characterised by severe optic neuritis and transverse myelitis. There are very few epidemiological studies in NMO and no randomised controlled studies that guide therapy. The aim of this review is to determine epidemiology of NMO and to provide an algorithm of treatment. **METHODS:** A systematic search was conducted of the relevant published evidence from Embase, MEDLINE, and Cochrane. Search limits were articles in English and in human. Retrieved citations were screened by two independent reviewers according to inclusion criteria: NMO, incidence, prevalence, and treatments reported in population base and observational studies. The analyses of comparable outcomes were carried out as per appropriate statistics along with critical appraisal of the studies. **RESULTS:** A total 16 studies met the inclusion criteria including six studies reported epidemiological data while 10 other studies reported treatment algorithm. Incidence of NMO ranged from 0.05 per 100,000 per year in United Kingdom (UK) to 0.4 per 100,000 in Southern Denmark. Prevalence was ranged from 0.44 per 100,000 in UK to 4.4 per 100,000 in Southern Denmark. Peak prevalence of NMO occurs among the people at 40-49 years of age. Low level evidence recommended methylprednisolone 1g/day for 3 to 5 days or 2 to 3 sessions of plasmapheresis per week, up to 7 sessions for acute attacks of NMO. Nine studies observed the improvements in the reduction of mean annualized relapse rate. **CONCLUSIONS:** There is limited evidence on current available treatment therapies for NMO. The available low level evidence found that high dose intravenous