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Efficacy of Satralizumab As Monotherapy in Pre-Specified Subgroups of Sakurastar, a Double-Blind Placebo-Controlled Phase 3 Clinical Study in Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD)

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Interleukin-6 (IL-6) is a pro-inflammatory cytokine implicated in the immune pathology of neuromyelitis optica (NMO) and NMO spectrum disorder (NMOSD). Satralizumab, a humanised recycling monoclonal antibody that binds to the IL-6 receptor, reduced risk of relapse in patients with NMO or NMOSD as add-on therapy in the SAkuraSky study (NCT02028884) and monotherapy in the SAkuraStar study (NCT02073279).

SAkuraStar is a randomised, double-blind, Phase 3 clinical trial comparing satralizumab monotherapy with placebo. 95 patients with NMO or NMOSD, with ≥1 documented relapse in the year prior to screening, were randomised to satralizumab (120 mg s.c.) or placebo. The primary endpoint was time to first protocol-defined relapse (PDR). Pre-specified subgroup analyses assessed treatment response by AQP4-IgG serostatus, prior therapy, and relapse history. Between-group hazard ratios (HRs) were based on Cox proportional hazards models.

Overall, satralizumab reduced risk of PDR by 55% vs placebo (n=95; HR 0.45; 95% confidence interval [CI] 0.23–0.89; p=0.018). There was a 74% reduction in PDR risk with satralizumab vs placebo in AQP4-IgG-seropositive patients (n=64; HR 0.26; 95% CI 0.11–0.63). In AQP4-IgG-seronegative patients, the HR was 1.19 (n=31; 95% CI 0.30–4.78). The proportions of AQP4-IgG-seropositive patients who were relapse-free at Weeks 48 and 96 were 82.9% and 76.5% on satralizumab, and 55.4% and 41.1% on placebo, respectively. In AQP4-IgG-seronegative patients, proportions were 63.3% and 63.3% on satralizumab, and 77.8% and 77.8% on placebo, respectively. In patients previously treated with B-cell depleting therapy, the HR for PDR was 0.72 (n=12; 95% CI 0.12–4.30) with satralizumab vs placebo. In patients on prior immunosuppressant or other NMO/NMOSD therapies, this HR was 0.42 (n=83; 95% CI 0.20–0.87). Patients with >1 relapse in the year prior to screening had a HR for PDR of 0.42 with satralizumab vs placebo (n=84; 95% CI 0.21–0.85); those with one relapse during screening had no change in PDR risk (n=11; HR: 1.00, 95% CI 0.09–11.02).

Satralizumab was effective in reducing risk of PDR in patients with NMO or NMOSD, particularly in AQP4-IgG-seropositive patients. The study was not powered for subgroup analyses; therefore, results should be interpreted with caution.

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Cladribine Tablets Are a Cost-Effective and Cost-Saving Treatment Strategy for High Disease Activity Relapsing Multiple Sclerosis Patients in Iran

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Cladribine tablets, hypothesized to act as an immune reconstitution therapy, are the first oral treatment for high disease activity relapsing multiple sclerosis (HDA-RMS). This study was conducted to assess the cost-effectiveness of cladribine tablets in comparison to natalizumab in HDA-RMS patients and also its budget impact in Iranian setting.

Cost-utility analysis (CUA): A Markov cohort model, with 21 expanded disability status scale (EDSS)-based health states was developed to compare cladribine tablets to natalizumab in a 5-year time horizon, from a societal perspective, in the context of Iran. Demographic and utility data were extracted from the CLARITY trial. Annual relapse rate and confirmed disability progression were extracted from a network meta-analysis, due to a lack of head-to-head trials. Mortality covariant such as age, sex and health states were also included. Effectiveness was assessed using quality adjusted life years (QALYs). Costs, which were identified through previous studies and expert opinion, were measured in Iranian Rial rates and converted to 2019 USD. Discount rates were 3.5% and 7.2% for QALY and costs, respectively. Probabilistic and deterministic sensitivity analyses (P/DSA) were conducted to assess robustness of the model.

Budget impact analysis (BIA): Markov-based static BIA was designed to compare total budgetary cost of two scenarios, with and without cladribine tablets, used in second-line treatment of RMS in a 10-year horizon. The Model was populated with the 2018 local MS pharmaceuticals usage data and included all available comparators (interferons, glatiramer acetate, dimethyl fumarate, teriflunomide, fingolimod and natalizumab). Key cost inputs included drug acquisition, administration and monitoring costs.

CUA: Cladribine tablets was superior to natalizumab and was associated with cost savings of 6.607 USD and increased QALY of 0.003 per patient, over a 5-year time horizon. Drug acquisition was the major cost component (92% in both arms). Results were robust in DSA and PSA (57.5% probability of cost-effectiveness at a willingness-to-pay threshold of 2,709 USD).

BIA: Considering a cohort of 35,667 patients, inclusion of cladribine tablets as a second-line RMS treatment will yield −0.33% savings in budget (7,856,019 USD), over a 10-year horizon.

Results indicated that use of cladribine tablets in HDA-RMS is a cost-effective and also cost-saving strategy in Iran.

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Efficacy of Satralizumab (SA237) As Add-on Therapy in Pre-Specified Additional Analyses of Sakurasky, a Double-Blind Placebo-Controlled Phase 3 Study in Patients with Neuromyelitis Optica Spectrum Disorders (NMOSD)

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A central role of interleukin-6 (IL-6) as key player in the pathophysiology of NMOSD, is strongly supported by the significant reduction in risk of relapse as previously demonstrated in the SAkuraSky study of the IL-6R inhibitor satralizumab for treatment of NMOSD as an add-on therapy. Here, we report the results of additional analyses (ClinicalTrials.gov number, NCT020728884).

83 patients meeting NMOSD diagnostic criteria with/without AQP4-Ab and at least two relapses in the last 2 years were randomly assigned to receive satralizumab 120 mg subcutaneously or placebo at week 0, 2 and 4 and every 4 weeks thereafter, added to stable immunosuppressant treatment. The primary endpoint was time to first protocol-defined relapse. Pre-specified additional analyses included efficacy in AQP4-Ab positive vs. negative subgroups, and effect on annualized relapse rate (ARR). Hazard ratios (HRs) were based on Cox proportional hazards model.

Satralizumab added to baseline treatment significantly reduced risk of protocol-defined relapse by 62% vs placebo; HR, 0.38; 95% confidence interval (CI), 0.16 to 0.88; P=0.0184. Pre-specified additional analyses showed a 79% relapse risk reduction with satralizumab vs placebo in AQP4-Ab(+) patients (n=55; HR, 0.21; 95% CI, 0.06 to 0.75) and 34% in AQP4-Ab(-) patients (HR 0.66; 95% CI, 0.20 to 2.24). In the overall study population, ARR was 0.11 (95% CI, 0.05 to 0.21) when treated with satralizumab vs 0.32 (95% CI, 0.19 to 0.51) with placebo.

Treatment with satralizumab as add-on to baseline immunosuppressant therapy significantly reduced relapse risk, particularly in AQP4-Ab(+) NMOSD patients.

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Fingolimod for Relapsing-Remitting Multiple Sclerosis: The Experience from Saudi Arabia

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Fingolimod (Gilenya, Novartis pharmaceuticals) is the first oral disease-modifying therapy for reducing the frequency of clinical relapses and delaying disability progression in patients diagnosed with relapsing-remitting multiple sclerosis (RRMS). In this study, we aim to evaluate the outcome of Saudi patients with active RRMS treated with fingolimod and compare the result with other studies.

We conducted a retrospective multicenter observational study involving 100 patients with RRMS at King Abdulaziz Medical City in Jeddah and Riyadh, Saudi Arabia. The inclusion criteria consisted of patients above the age of 18 years, diagnosed with RRMS according to the revised McDonald criteria, and are currently receiving or received fingolimod treatment in the past for a minimum of six months.

The mean baseline expanded disability status scale (EDSS) score was 2.95±2.58 (range 1-7; median 1.75). The mean EDSS score at last follow up was 2.95±2.65 (range 1-10; median 2.00). The mean annualized relapse rate (ARR) was significantly reduced from 1.24±1.39 at baseline to 0.43±1.15 at the last follow-up (P = 0.001). In addition, radiological activity was significantly improved at follow-up magnetic resonance imaging (MRI) studies when compared to the baseline.

Our multi-center study provides further evidence on the efficacy of fingolimod in reducing clinical and radiological disease activity in patients with RRMS. The reduction in relapse rate, stabilization of EDSS score, and improvement in MRI images were similar to other observational studies conducted in different countries worldwide. Fingolimod appears to be a well-tolerated for our MS population.

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The Use Natalizumab in Multiple Sclerosis Patients During Pregnancy is Safe and Prevents Disease Reactivation

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Data of the use of natalizumab during pregnancy is limited in Multiple Sclerosis (MS) patients. We aimed to assess the effectiveness and safety of natalizumab in MS during pregnancy.

The cohort constituted 3 groups; patients continued natalizumab during pregnancy till 28th gestational week (group 1), patients discontinued natalizumab before pregnancy (group 2) and a control group included women who did not get pregnant (group 3). Relapses and MRI new T2/ gad-enhancing lesions during pregnancy and at one-year post delivery were compared.

68 patients were identified. At baseline, there were no significant differences across the three groups in mean age (p = 0.07), mean age at onset (p = 0.44), mean disease duration (p = 0.21), annualized relapse rate (p = 0.27) and MRI measures (p = 0.25). The mean number of natalizumab infusions was 44 ± 26.05. During pregnancy, no relapses occurred in group 1 while four patients (28.6%) sustained relapses in group 2 (p = 0.03). At last follow-up visit, annual relapse rate was significantly higher in group 2 (0.75 ± 0.51), compared to groups 1 & 3 (0.14 ± 0.36 & 0.05 ± 0.22; p < 0.001) respectively. The proportion of patients with MRI activity was significantly higher in group 2 compared to groups 1 and 3 (50%, 7.1%, and 2.5%; p = 0.03). Abortion rate was not statistically significant between group 1 and 2 (p = 0.47) and no fetal malformation was observed.

Patients who continued using natalizumab during pregnancy remained in remission. The use of natalizumab during pregnancy was safe.

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Pregnancy Outcome in Multiple Sclerosis Patients Exposed to Disease Modifying Therapies

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