443 patients (mean age=46.1 years; female=57.3%) and AP cohort included 4,374 patients (mean age=44.8 years; female=59.1%). At month 6 pre-index, ESK cohort had a mean of 1.7 MH-related disability days PPPM relative to 1.2 days in the TMS, 1.3 days in the ECT, and 0.8 days in the AP cohort while mean MH-related disability costs were $443 PPPM in the ESK cohort relative to $178 in the ECT, $339 in the TMS, and $143 in the AP cohort.

In all cohorts, mean MH-related disability days and costs peaked at month 1 after therapy initiation followed by a decreasing trend. At month 6 post-index versus month 6 pre-index, the mean number of MH-related disability days decreased by 0.4 days PPPM in the ESK cohort, remained the same in the TMS cohort, and increased by 1.6 and 0.1 days in the ECT and AP cohorts, respectively. In the same timeframe, MH-related disability costs decreased by $312 and $123 PPPM in the ESK and TMS cohorts and increased by $353 and $26 in the ECT and AP cohorts, respectively. MH-related disability days and costs were driven primarily by short-term disability.

Conclusion. In this descriptive analysis, mean MH-related disability days and costs trended higher at month 6 before therapy initiation in ESK relative to TMS, ECT, and AP cohorts. ESK initiation was associated with lower mean MH-related disability days and costs at month 6 after versus before initiation. This trend was either not observed or less pronounced among patients with TRD initiated on conventional therapies. Results suggest potential economic and societal gains associated with ESK treatment for TRD.

Funding. Janssen Scientific Affairs, LLC

Adverse Event Duration with Esketamine Versus Quetiapine XR in Adults With Treatment-Resistant Depression: A Subgroup Analysis of ESCAPE-TRD

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Introduction. In ESCAPE-TRD (NCT04338321), a randomized, open-label, rater-blinded, long-term, phase 3b trial, augmentation with esketamine nasal spray (ESK) demonstrated increased probability of achieving meaningful clinical benefit versus quetiapine extended release (QUE XR) in patients (pts) with treatment-resistant depression (TRD). This subgroup analysis of ESCAPE-TRD evaluated the incidence, duration, and impact of treatment-emergent adverse events (TEAEs) on treatment discontinuation in adults with TRD treated with ESK or QUE XR according to US prescribing information.

Methods. Pts aged 18-64 years were randomly assigned to receive flexibly dosed ESK (56 or 84 mg) or QUE XR (150-300 mg), both consistent with US label dosing and in combination with an ongoing oral antidepressant. The incidence and duration of the most commonly occurring TEAEs, as well as the most common TEAEs leading to treatment discontinuation, were summarized descriptively. All randomly assigned participants receiving ≥1 dose of study drug were included in the safety analyses.

Results. Among the 636 pts included in the subgroup analysis, 316 and 320 were randomly assigned to ESK and QUE XR, respectively; 314 and 316 were included in the safety population. In the combined acute and maintenance phases, TEAEs occurred in 92.0% of pts in the ESK group and 78.5% of pts in the QUE XR group. The most commonly reported TEAEs with ESK or QUE XR in the combined acute and maintenance phases were dizziness (47.1% and 7.9%, respectively), headache (25.5% and 13.0%, respectively), somnolence (15.0% and 23.4%, respectively), and nausea (29.9% and 3.2%, respectively). Across all TEAE events reported in ≥5% of pts in either arm, 91.8% (5831 of 6351) resolved within 1 day in the ESK arm compared to 11.6% (90 of 776) with QUE XR. For specific TEAE events of clinical interest for ESK, same-day resolution rates for increased blood pressure, sedation, and dissociation in the ESK group were 93.5% (116 of 124), 96.2% (127 of 132), and 99.6% (740 of 743), respectively. The majority of TEAEs of clinical interest in the ESK group that occurred on the same day of dosing resolved within the first 2 hours after dosing. For the most frequently reported TEAEs with QUE XR, same-day resolution rates for somnolence, headache, and fatigue were 7.8% (8 of 103), 49.2% (29 of 59), and 9.5% (4 of 42), respectively. Fewer pts treated with ESK discontinued treatment due to TEAEs compared to QUE XR (4.4% versus 10.6%).

Conclusions. Safety data from this subgroup analysis were consistent with the overall study population as well as the known tolerability profile of each treatment. TEAEs were reported at higher incidence with ESK than with QUE XR; however, the majority of TEAEs occurring with ESK were transient in nature and did not result in a higher rate of treatment discontinuation compared to QUE XR.

Funding. Janssen Scientific Affairs, LLC

Cost Efficiency of Esketamine Nasal Spray Versus Quetiapine for Treatment Resistant Depression

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Objective. To compare the per-patient direct and indirect costs associated with achieving remission with esketamine nasal spray

https://doi.org/10.1017/S1092852924002104 Published online by Cambridge University Press

plus oral antidepressants (ESK NS+OAD) versus quetiapine extended release plus oral antidepressants (QTP XR+OAD) among patients with treatment-resistant depression (TRD). This comparison was based on a subanalysis of results from the ESCAPE-TRD Phase 3b trial (ex-US) comparing response and remission rates for ESK NS+OAD vs QTP XR+OAD in TRD patients over 32 weeks.

Methods. An Excel-based model was developed to estimate the cost-per-remitter for ESK NS+OAD and QTP XR+OAD from the perspective of a commercial insurance plan in the US. Remission rates, response rates, and relapse rates (among patients remitting or responding during the first 8 weeks of treatment) were estimated in 4-week intervals over 32 weeks using data from the ESCAPE-TRD Phase 3b clinical trial comparing ESK NS+OAD versus QTP XR+OAD in patients with TRD. Patients not remitting/responding (non-responders) or experiencing a relapse either stayed on current treatment (i.e., ESK NS+OAD or QTP XR+OAD) or discontinued current treatment and initiated either augmented therapy with antipsychotics (APS) or recurring transcranial magnetic stimulation (rTMS). For basecase analysis, equal proportions of non-responders off-treatment initiated rTMS or augmented therapy with APS. In a scenario analysis, all non-responders off-treatment initiated rTMS. Direct costs, including medical and drug costs, were derived from health economic literature and the RED BOOK® drug pricing database. Indirect costs attributed to work productivity loss from presenteeism and absenteeism were derived from a separate analysis of ESCAPE-TRD patients using the Work Productivity and Activity Impairment: Depression (WPAI:D) questionnaire and US Bureau of Labor Statistics survey results.

Results. The cumulative relapse-free remission rate at 32 weeks was 50% for patients receiving ESK NS+OAD and 33% for patients receiving QTP XR+OAD. In the basecase analysis, the cost-per-remitter (including direct and indirect costs) for ESK NS +OAD was $3,102.17 lower than that of QTP XR+OAD. In the scenario where 100% of non-responders off-treatment were assumed to initiate rTMS, the cost-per-remitter (including direct and indirect costs) for ESK NS+OAD was $15,133.66 lower than that of QTP XR+OAD.

Conclusion. These findings suggest that esketamine nasal spray in conjunction with oral antidepressants is a cost-efficient alternative compared with quetiapine extended release for treatment of TRD for commercial insurance plans. The comparative benefits associated with ESK NS+OAD treatment are driven primarily by better short- and long-term efficacy observed in the trial and particularly pronounced when considering the costs associated with lost productivity.

Funding. Janssen Scientific Affairs, LLC

Effectiveness of Esketamine as a Treatment for Depression: A Real-World Survey of Disease Improvement

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Introduction. Major depressive disorder (MDD) is the second leading cause of disability in the US, and increases the risk of poor health outcomes. This analysis assessed the real-world benefit and availability of esketamine for patients with difficult-to-treat-MDD.

Methods. Data were drawn from the Adelphi Real World Depression Disease Specific Programme XII (DSP™), a cross-sectional retrospective survey of physicians and their patients in the United States in 2022. Physicians reported details for patients with MDD receiving esketamine regarding their prescribed medication (including access), daily functioning and disease improvement whilst receiving esketamine (reported by Clinical Global Impression Improvement Scale (CGI-I)),)) change in depression severity (reported by Clinical Global Impression Severity Scale (CGI-S)) and physician satisfaction. CGI-I responses measured level of disease improvement since the initiation of current depression treatment regimen ('Very much worse=1' to 'Very much improved=7'). CGI-S response options were converted to numerics to measure level of severity change ('Normal, not at all ill=0' to 'Among the most extremely ill patients=6') and compared at time of esketamine initiation and currently. Physician satisfaction with medication's ability to achieve patient treatment goals was derived from a numeric scale (where 'Not at all satisfied=1' to 'Very satisfied=5').

Results. 94 patients with MDD were currently receiving esketamine. Mean age was 44.3 (SD 13.26) and 47% were male. 26% of patients had been receiving esketamine for 0-3 months, 5% for 3-6 months, 15% for 6-12 months, 23% for 1-2 years and 30% for more than 2 years. CGI-I results showed physicians rated depression as improved in 98% of patients receiving esketamine >30 days. CGI-S results showed that patients receiving esketamine 1-30 days had a mean improvement of 1.2 while patients receiving esketamine for >30 days showed mean improvement of 0.9. 80% of physicians reported high satisfaction (score of 4 or 5) with esketamine's ability to achieve patient treatment goals.

In patients receiving esketamine >30 days physicians reported that 62% could function better socially, 53% had a better quality of life, 41% had increased ability to work, 37% could better meet their own basic needs and 34% had an improvement in overall general health.

When prescribing esketamine, the treatment was only "available without restrictions" for 18% of patients, whilst 82% experienced at least some restrictions.

https://doi.org/10.1017/S1092852924002104 Published online by Cambridge University Press