Long-Term Effectiveness With Subcutaneous Long-Acting Injectable Olanzapine (TV-44749) in Adults With Schizophrenia: Results From up to 48 Weeks Open-Label Treatment in the Phase 3 SOLARIS Trial

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Objective: To assess the long-term clinical effectiveness of TV-44749 in adults with schizophrenia during the open-label, long-term safety period ⩽48 weeks; Period 2 of the SOLARIS trial.

Background

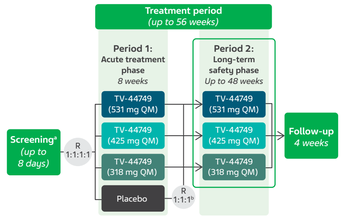
- Long-acting injectable (LAI) antipsychotics demonstrate improved adherence and outcomes in adults with schizophrenia.[1-3]
- The second-generation antipsychotic olanzapine is available as an intramuscular LAI olanzapine pamoate; however, risk of post-injection delirium/sedation syndrome (PDSS) and the associated Risk Evaluation and Mitigation Strategy (REMS) requirements limits its use.[4,5]
- TV-44749 is an innovative, once-monthly, subcutaneous LAI olanzapine designed to provide sustained efficacy over the monthly dosing interval and avoid the risk of PDSS.
- SOLARIS (NCT05693935) was a phase 3 trial assessing efficacy, safety, and tolerability of TV-44749 in adults with acute exacerbation of schizophrenia.[6,7]
  - Results from the 8-week, placebo-controlled Period 1 demonstrated significantly greater efficacy with TV-44749 versus placebo, with no new safety signals identified and no reported (suspected or confirmed) cases of PDSS.
  - TV-44749 met all primary and key secondary (type-I error controlled) endpoints during Period 1.

Methods

SOLARIS trial design and participants (Figure 1)

- SOLARIS comprised an 8-week, randomized, double-blind, placebo-controlled period (Period 1), followed by an open-label period of up to 48 weeks (Period 2).

Figure 1: SOLARIS trial study design



[a]Participants entering the trial who had not previously received oral olanzapine within the last year received 2 oral doses of olanzapine for 2 consecutive days at the screening period to assess tolerability. The investigator verified the previous use, tolerability, and duration of olanzapine treatment to assure prior tolerability.

[b]To maintain the blinding in Period 1, all participants were rerandomized between Periods 1 and 2; participants previously assigned to the active treatment groups retained their Period 1 treatment assignment (rerandomization was done to maintain blinding of Period 1, and de facto is a deterministic assignment and not randomization), and participants previously assigned to placebo were randomized to one of the active treatment groups in a 1:1:1 ratio. Participants were hospitalized for ⩾28 days after receiving the first injection.

QM, once monthly; R, randomization.

- Participants (aged 18–64) with acute exacerbation of schizophrenia starting ⩽8 weeks before screening who would benefit from hospitalization (or continued hospitalization) were randomized.
- In Period 2 (n=423), Period 1 TV-44749 participants retained their treatment, and those previously assigned placebo were rerandomized 1:1:1 to TV-44749 (318 mg, 425 mg, or 531 mg). Selected TV-44749 doses were comparable to daily oral olanzapine doses of 10 mg, 15 mg, and 20 mg.

Period 2 long-term clinical effectiveness outcomes

- Change in Positive and Negative Syndrome Scale (PANSS) total, Clinical Global Impression-Severity (CGI-S), and Personal and Social Performance (PSP) scale scores were assessed from Period 2 baseline (first TV-44749 use in Period 2, at week 8) to end of treatment (EoT):
  - In participants who completed EoT at any time (visit performed 4 weeks after last dose in Period 2).
  - In participants who completed EoT after receiving ⩾10 TV-44749 injections in Period 2.

Statistical analysis

- A repeated measures model was used, with treatment, trial visit, treatment visit interaction, stratification variables (sex and geographic region), age, and efficacy measure score at baseline as covariates.
- Each treatment group must have had ⩾10 participants per visit to be included in the model.

Acknowledgments

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Disclosures

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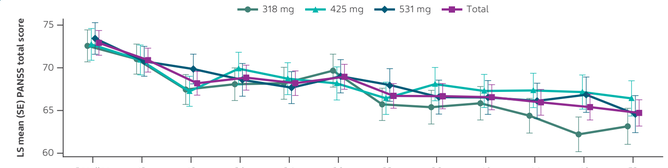
Results

SOLARIS Period 2 participants

- Overall, 423 participants were included in Period 2 (**Supplemental Figure 1**):
  - TV-44749 318 mg, n=140; TV-44749 425 mg, n=142; TV-44749 531 mg, n=141 (n=40, n=35, n=29 were rerandomized from placebo in Period 1, respectively).
- Baseline demographics and disease characteristics were comparable across TV-44749 groups (**Supplemental Table 1**):
  - 72% were male and the mean age was 44.8 years.
  - 67% were Black or African American and 79% were not Hispanic or Latino.
  - Mean disease duration was 19.5 years.
  - Mean (SD) baseline PANSS total score was 74.7 (16.60), CGI-S scale score was 3.7 (0.92), and PSP scale score was 61.9 (11.64).

TV-44749 demonstrated long-term clinical effectiveness.

Figure 2: Mean PANSS total score from baseline[a] by visit and treatment group (full analysis set)



Participants (n)

318 mg	135	118	99	84	74	69	58	55	52	50	49	46
425 mg	138	117	96	80	73	69	62	63	56	56	54	53
531 mg	137	110	96	76	71	58	52	49	45	43	43	39
Total	410	345	291	240	218	196	172	167	153	149	146	138

[a]Baseline refers to Period 2 baseline at week 8 (visit 11).
LS, least squares; SE, standard error.

Conclusions

- All TV-44749 doses exhibited long-term, continuous symptom improvement and maintenance of clinical effectiveness in Period 2 of the SOLARIS trial.
- Participants assigned to placebo in Period 1 showed greater improvements in Period 2 due to higher baseline severity, but both groups ultimately achieved similar absolute scores across all efficacy scales by EoT regardless of treatment assignment in Period 1.
- TV-44749 provides long-term, effective subcutaneous LAI olanzapine treatment for adults with schizophrenia with no suspected or confirmed PDSS events following 3740 injections.

Table 1: Changes in symptom and functioning assessment scales from Period 2 baseline to EoT at any time and in participants with ⩾10 TV-44749 injections (full analysis set)

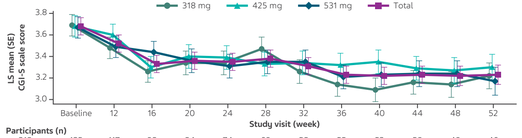
Mean (SD)	TV-44749 318 mg	xPlc/ TV-44749 318 mg	TV-44749 425 mg	xPlc/ TV-44749 425 mg	TV-44749 531 mg	xPlc/ TV-44749 531 mg	TV-44749 Total
PANSS Total score							
Score at Period 2 baseline (n=410)	71.0 (15.47)	81.2 (16.25)	71.8 (15.57)	82.1 (17.83)	72.8 (15.05)	83.6 (21.59)	74.5 (16.65)
Change from baseline to EoT at any time (n=238)	−4.6 (15.64)	−14.8 (20.45)	−4.7 (13.70)	−8.1 (16.46)	−4.8 (12.09)	−24.6 (23.24)	−7.2 (16.21)
Change from baseline to EoT for participants who received ⩾10 TV-44749 injections (n=137)	−4.7 (17.55)	−19.0 (21.84)	−4.3 (13.92)	−12.2 (18.87)	−7.9 (9.89)	−27.6 (21.26)	−8.9 (17.09)
CGI-S scale score							
Score at Period 2 baseline (n=410)	3.6 (0.94)	4.1 (0.96)	3.6 (0.88)	4.2 (0.95)	3.6 (0.77)	4.0 (1.23)	3.7 (0.93)
Change from baseline to EoT at any time (n=239)	−0.3 (0.97)	−1.0 (1.30)	−0.4 (0.85)	−0.5 (0.77)	−0.3 (0.75)	−1.2 (1.48)	−0.5 (0.98)
Change from baseline to EoT for participants who received ⩾10 TV-44749 injections (n=138)	−0.3 (1.10)	−1.1 (1.28)	−0.3 (0.92)	−0.8 (0.83)	−0.4 (0.67)	−1.3 (1.41)	−0.5 (1.03)
PSP scale score							
Score at Period 2 baseline (n=410)	64.5 (11.69)	58.5 (10.36)	62.1 (12.69)	59.4 (11.03)	62.4 (10.50)	58.6 (13.33)	61.9 (11.71)
Change from baseline to EoT at any time (n=239)	3.6 (10.73)	8.7 (15.72)	3.2 (10.56)	4.3 (10.27)	3.8 (10.99)	11.7 (14.91)	4.6 (11.72)
Change from baseline to EoT for participants who received ⩾10 TV-44749 injections (n=138)	3.6 (10.88)	12.3 (16.90)	2.8 (11.32)	4.0 (6.95)	6.3 (7.80)	12.9 (15.24)	5.6 (11.64)

Baseline refers to Period 2 baseline at week 8 (Visit 11).
xPlc, ex-placebo; EoT, end of treatment.

Long-term effectiveness of TV-44749 from baseline through EoT at any time

- TV-44749 demonstrated long-term clinical effectiveness with stable improvements in PANSS total score (n=137), CGI-S scale score (n=138), and PSP scale score (n=138) from Period 2 baseline through EoT (**Table 1**).
- All TV-44749 groups showed a reduction in LS mean (SE) PANSS total and CGI-S scale scores to week 52 (**Figures 2 and 3**).
  - In all dose groups, reductions were sustained through Period 2.
- All TV-44749 groups showed a sustained increase in LS mean (SE) PSP scale score through EoT (**Figure 4**).

Figure 3: Mean CGI-S scale score from baseline[a] by visit and treatment group (full analysis set)



Participants (n)

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425 mg	138	117	96	80	73	69	62	63	56	56	54	53
531 mg	137	110	96	76	71	58	52	49	45	43	43	39
Total	410	344	290	240	218	196	172	167	153	149	146	138

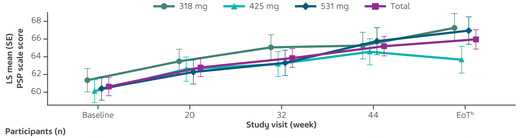
[a]Baseline refers to Period 2 baseline at week 8 (visit 11).

- During Period 2, change from baseline in PANSS and CGI-S scores to EoT were higher for participants who received placebo in Period 1 compared with participants who received TV-44749 in Period 1 (**Table 1**). Similar results were demonstrated in participants who received ⩾10 TV-44749 injections in Period 2.

Long-term effectiveness of TV-44749 from baseline to EoT after receiving ⩾10 TV-44749 injections in Period 2

- All TV-44749 groups showed a reduction in mean (SD) PANSS total and CGI-S scale scores from Period 2 baseline to EoT in participants with ⩾10 TV-44749 injections (**Table 1**).
- All TV-44749 groups showed a sustained increase in mean (SD) PSP scale score from Period 2 baseline to EoT in participants with ⩾10 TV-44749 injections (**Table 1**).

Figure 4: Mean PSP scale score from baseline[a] to EoT by visit and treatment group (full analysis set)



Participants (n)

318 mg	135	84	59	50	48
425 mg	138	83	61	55	49
531 mg	137	80	52	43	41
Total	410	247	172	148	138

[a]Baseline refers to Period 2 baseline at week 8 (visit 11). [b]Refers to participants who received ⩾10 injections in Period 2 and completed EoT visit.

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