

ORAL PRESENTATION

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Once-daily S/GSK1349572 combination therapy in antiretroviral-naïve adults: rapid and potent 24-week antiviral responses in SPRING-1 (ING112276)

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Purpose of study

S/GSK1349572, a next-generation HIV-1 integrase inhibitor, has previously demonstrated potent antiviral activity in Phase 2a with once-daily, unboosted dosing. SPRING-1 is an ongoing dose-ranging study designed to select a dose to for Phase 3 evaluation.

Methods

SPRING-1 is a Phase 2b, multicentre, partially-blinded study in therapy-naïve adults, randomized 1:1:1:1 to 10mg, 25mg or 50mg of S/GSK1349572 or efavirenz (EFV) 600mg once-daily with either co-formulated TDF/FTC or ABC/3TC.

Summary of results

205 subjects received study drug: 86% male, 20% non-white, 26% >100,000c/mL HIV-1 RNA, 67% TDF/FTC. Plasma HIV-1 RNA declined rapidly across all S/GSK1349572 doses with no differences in NRTI subgroups. Three protocol-defined virologic failures occurred, 1 on EFV (<1log₁₀ decline by Week 4), and 2

on S/GSK1349572 (Week 4 and 24 rebound >400c/mL with no INI mutation detected). No dose-related clinical or laboratory toxicities were observed. More drug-related AEs of moderate-or-higher intensity were reported on EFV (20%) than S/GSK1349572 (6%) arms; none occurred in more than 1 S/GSK1349572 subject. The most frequent category of such events reported by subjects receiving EFV and S/GSK1349572 were gastrointestinal (4% vs. 2%, respectively); other frequent events on EFV were psychiatric (6%) and rash (4%) disorders. No SAE was considered related to S/GSK1349572. Six subjects (2: S/GSK1349572 and 4: EFV) withdrew due to AEs. Mean change from baseline in LDL cholesterol was +0.023mmol/L among S/GSK1349572 subjects and +0.468mmol/L among EFV subjects. S/GSK1349572 demonstrated low pharmacokinetic variability and drug exposure increased with dose. Table 1

Conclusions

S/GSK1349572 administered once-daily without a PK booster was well tolerated with potent antiviral activity

Table 1

Planned Week 24 Interim Analysis Results	S/GSK1349572 10 mg (n=53)	S/GSK1349572 25mg (n=51)	S/GSK1349572 50mg (n=51)	EFV control (n=50)
Mean baseline HIV-1 RNA (log ₁₀ c/mL)	4.42	4.38	4.58	4.46
%<50c/mL at 24 wks (by TLOVR)	96% (51/53)	90% (46/51)	92% (47/51)	78% (39/50)
Median baseline (change from baseline at 24 weeks) CD4 + cells/mm ³	289 (+159)	330 (+206)	305 (+167)	308 (+110)†

†p=0.008; Wilcoxon two-sample test vs. S/GSK1349572 arms (median change: +176)

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at all doses explored in SPRING-1. The greater CD4+ cell increases on S/GSK1349572 merit further observation and confirmation.

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