CABOTEGRAVIR + RILPIVIRINE EVERY 2 MONTHS IS NONINFERIOR TO MONTHLY: ATLAS-2M STUDY

Abstract Body

The 2-drug regimen of long-acting (LA) cabotegravir (CAB) and rilpivirine (RPV) dosed i.m. every 4 weeks (Q4W) was noninferior to daily oral 3-drug ART in Phase 3 studies. These results and supportive CAB+RPV LA pharmacokinetics enable regimen evaluation at a longer and potentially more convenient 8-week dosing interval (Q8W).

ATLAS-2M is a multicenter, open-label, Phase 3b noninferiority (NI) study of CAB+RPV LA maintenance therapy administered Q8W (600mg CAB + 900mg RPV) or Q4W (400mg CAB + 600mg RPV) to treatment-experienced, HIV-infected adults. Virologically suppressed individuals on CAB+RPV LA Q4W (ATLAS study rollover) or oral standard-of-care were randomized 1:1 to receive CAB+RPV LA Q8W or Q4W. The primary endpoint at Week 48 was the proportion with plasma HIV-1 RNA ≥50 c/mL (Snapshot, ITT-exposed [ITTe]) with an NI margin of 4%. The key secondary endpoint was the proportion with HIV-1 RNA <50 c/mL (Snapshot, ITTe) with an NI margin of -10%.

1045 participants were randomized and treated with CAB+RPV LA Q8W (n=522) or Q4W (n=523); 27% were female, 73% were white. Median age was 42 years (range 19–83); 63% were naïve to CAB+RPV LA while 37% transitioned from Q4W CAB+RPV LA in ATLAS. CAB+RPV LA Q8W was noninferior to Q4W dosing in both the primary (1.7% vs 1.0%) and secondary analysis (94.3% vs 93.5%; see Table). There were 8 and 2 confirmed virologic failures (CVFs; 2 sequential measures ≥200 c/mL) on Q8W and Q4W dosing, respectively; 5 and 0 CVFs, respectively, had archived resistance-associated mutations (RAMs) to RPV (E138A, Y188L, H221Y, Y181C) either alone (n=4) or with a CAB RAM (G140R, n=1) in baseline Peripheral blood mononuclear cells (PBMCs). On-treatment RAMs to RPV (K101E, E138K, M230L), CAB (N155H, Q148R, E138K), or both not present in baseline PBMCs were found in 5/8 Q8W CVFs and both Q4W CVFs. The safety profile was similar for Q4W and Q8W dosing (Table). Injection site reactions (ISRs) were mostly mild or moderate (98% overall) with a median duration of 3 days. Discontinuation for an adverse event occurred in 2% of patients (Q8W, n=12; Q4W, n=13), with 5 (1%) in each group due to ISRs. There was one death (Q8W; sepsis). Of those treated Q8W in ATLAS-2M after ≥48 weeks of Q4W dosing in ATLAS, 93% (115/124) expressed a preference for Q8W dosing.

Q8W dosing of CAB+RPV LA was noninferior to Q4W dosing and well tolerated. These results support the therapeutic potential of CAB+RPV LA administered every 2 months.

CONFERENCE DATES AND LOCATION

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