Phase 3 comparison of lopinavir/ritonavir vs. investigator-selected protease inhibitors in single PI-experienced, NNRTI-naive patients: 48-week results of study M98-888

RB Pollard (1), M Thompson (2), C Hicks (3), B Grinsztejn (4), A Horban (5), P Cernohous (6), J Omachi (6), M Norton (6), M King (6), S Brun (6).

(1) University of California, Davis Medical Center, (2) AIDS Research Consortium of Atlanta, (3) Duke University Medical Center, (4) Hospital Evandro Chagas-Fiocrnz, Brazil (5) AIDS Diagnosis and Therapy Center of Warsaw, (6) Abbott Laboratories, USA.

Background. In a phase 2 trial in single PI-experienced patients(pts), lopinavir/ritonavir(LPV/r) plus nevirapine(NVP) and 2 NRTIs demonstrated durable antiviral activity through three years.

Methods. In a phase 3, randomized, open-label, 48-week trial, 288 NNRTI-naive pts failing an initial PI-based regimen(HIV RNA 1,000-500,000 c/mL) received LPV/r 400/100 mg BID(n=148) or investigator-selected protease inhibitors(n=140, ISPIs). Allowed control-arm PIs were any single PI, RTV/SQV(400/400), RTV/IDV(400/400), or NFV/SQV(1250/1200). All pts received NVP and 2 NRTIs.

Results. Pts were primarily male(86%) and Caucasian(80%), with a mean age of 40. Mean baseline HIV RNA and CD4 count were 4.1 $\log_{10}$c/mL and 322 cells/mm^3. The most common prior PIs were NFV(43%) and IDV(42%). ISPIs regimens included RTV/SQV(44%), RTV/IDV(21%), and NFV (21%). Discontinuation through 48 weeks was 43% for ISPIs(14% AE, 13% virologic failure (VF), other 16%) and 24% for LPV/r(5% AE, 2% VF, other 17%), $p<0.001$. By intent-to-treat analysis, 57%(LPV/r) and 33%(ISPIs) had HIV RNA <400 c/mL at 48 weeks (FDA time to loss of virologic response algorithm, $p<0.001$). As in prior LPV/r trials, LPV/r-treated pts with 0-3 PI mutations at positions 10,20,24,33,36,47,48,54,82,84 had better virologic response vs. those with $\geq$4 mutations($p=0.027$). CD4 count increases through 48 weeks were 111 (LPV/r) and 112 (ISPIs) cells/mm^3. The most common moderate/severe, drug-related AEs and grade 3 lab elevations were nausea (7% LPV/r, 16% ISPIs), vomiting (4% LPV/r, 12%, ISPIs), diarrhea (7% LPV/r, 9% ISPIs), total cholesterol (>300 mg/dL, 20% LPV/r, 21% ISPIs) and triglycerides (>750 mg/dL, 25% LPV/r, 21% ISPIs).

Conclusions. While study limitations include control arm dose combinations less commonly used today, a LPV/r-based regimen demonstrated superior virologic efficacy and better tolerability in single PI-experienced pts, vs. a regimen based on investigator-selected PIs.