Catherine Hill: None declared, Lyn March Speakers bureau: Speaker fees from Pfizer Australia Ltd, Bristol Myer Squibb Australia, Abbvie Australia, Grant/ research support from: Grant support for my institution from Janssen for unrelated research. None declared, Patrick Otah: None declared, Flavia Cicuttini: None declared, Graeme Jones: None declared

DOI: 10.1136/annrheumdis-2021-eular.4424

ANABOLIC EFFECT OF LNA403, A NOVEL DISEASE-MODIFYING OSTEOARTHRITIS DRUG CANDIDATE: RESULTS FROM AN IMAGING-BASED PROOF-OF-CONCEPT TRIAL IN PATIENTS WITH FOCAL ARTICULAR CARTILAGE LESIONS


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Background: LNA403 is a modified, recombinant version of the human angiopoietin-like 3 (ANGPTL3) protein acting directly on cartilage-resident cells to transduce anabolic signalling. In a 5-year, pooled, observational study that evaluated the safety and exploratory efficacy of a single LOR injection that was previously administered into the target knee joint of subjects with moderate to severe knee OA, the study was terminated in its third year, as relevant long-term safety information became limited in the absence of repeated LOR administration. The primary objective evaluated the incidence of serious adverse events (SAEs), safety data for all doses and a post hoc efficacy analysis for the pivotal dose (0.07 mg LOR) are reported.

Methods: This was a Phase 3, multicenter, observational, extension study of completers subjects (OA-05; NCT02951026) from two Phase 2 trials of LOR: a 12-month Phase 2a trial (OA-02; NCT2536833) and a 6-month Phase 2b trial (OA-04; NCT03122860). Subjects received a single LOR or control (placebo or vehicle) injection at their parent-study baseline visit (OA-02 or OA-04 Visit 0 in this analysis). Pooled data from clinic visits at 6, 12, 24, and 36 months contributed to the extension-study (OA-05) analysis. SAEs, knee-related adverse events (AEs), and AEs of newly diagnosed conditions requiring treatment were collected as safety outcomes. Efficacy was assessed by target knee WOMAC Pain and Function subscores and radiographic medial joint space width (mJSW). A post hoc analysis was performed for 0.07 mg LOR versus control to assess responses in a subject subgroup (unilateral symptoms, no widespread pain, 18-month post-injection radiograph at study termination). Baseline-adjusted ANCOVA was performed using data from both the current and parent studies at 0, 3, 6, 12, and 18 months.

Results: Of 703 subjects, 119 (17%) subjects discontinued prior to study termination. Subjects had a mean age of 60.7 years and mean BMI of 29.1 kg/m², and 61% were female. The majority of subjects had K/L 3 (61.2%) OA. The safety analysis set included 495 LOR-treated subjects and 208 control subjects.