TPS12149 Poster Session

Epidermal growth factor receptor (EGFR) inhibitor-induced dermal toxicity treated with topical application of a novel Staphylococcus epidermidis compound.

Mary C. Spellman, Travis C. Whitfill; Panclarity LLC, San Francisco, CA; Azitra Inc, Branford, CT

Background: Agents targeting the EGFR-mediated signaling pathway are used for the treatment of advanced lung, pancreatic, colorectal, and head and neck cancers. Significant dermal toxicities, occurring in up to 90% of patients treated with EGFR inhibitors (EGFRIs) and other medications inhibiting downstream signaling pathways, may be disruptive to a patient's quality of life and adherence to therapy. Inhibition of the EGFR pathway may suppress host defenses and lead to opportunistic pathogenic colonization or infection. Dermal toxicity is associated with elevated levels of Staphylococcus aureus and IL-36γ. ATR04-484 is an S. epidermidis strain isolated from a healthy human volunteer, selected for its ability to reduce S. aureus colonization and inhibit IL-36γ when applied topically. Reconstructed human epidermis (RHE) and ex vivo pig skin were utilized to measure the effect of ATR04-484 on S. aureus in therapeutic and prophylactic settings with S. aureus added prior to or after ATR04-484, respectively. ATR04-484 inhibited growth of both methicillin-resistant (MRSA) and methicillin-sensitive (MSSA) S. aureus in both therapeutic and prophylactic settings. IL-36γ levels were measured on RHE treated with erlotinib alone or in combination with ATR04-484. Application of ATR04-484 reduced erlotinib-induced IL-36γ to a level comparable to non-erlotinib treated RHE. The effect was dose-dependent; application of 10^9CFU/cm^2 of ATR04-484 showed more potent IL-36γ reduction compared to 10^8 CFU/cm^2. ATR04-484 has a promising profile of activities for the treatment of EGFRI-induced dermal toxicity by significantly reducing *S. aureus* growth and completely ameliorating IL-36γ levels. **Methods:** This multicenter, randomized, double-blind, vehicle-controlled Phase 1/2 clinical study is designed to evaluate the safety and tolerability of topical ATR04-484 (10^9 CFU/g) for the treatment of EGFRI associated dermal toxicity affecting the face of adult patients. ATR04-484 or its vehicle (3:1 randomization) will be applied in a stable volume to all patients and may include application to prioritize affected areas of the neck, chest, back, and paronychial areas (using remaining product on unaffected skin in the same areas, as needed). The key objectives of the study are to assess the safety and tolerability of topical ATR04-484 and to evaluate efficacy signals including severity of disease, pruritus, and pain. The bioavailability of ATR04-484 and pharmacodynamic parameters (including IL-36γ) are also studied. This clinical study will establish the basis for continued clinical development of ATR04-484. Clinical trial information: not yet assigned. Research Sponsor: Azitra Inc.