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**Investigator assessment of the efficacy of sonidegib 200 mg once daily and concordance rates with assessments by central review in patients with locally advanced basal cell carcinoma: Results of the 42-month randomized double-blind BOLT study**

Michael Migden, MD, University of Texas, MD Anderson Cancer Center, Department of Dermatology, Division of Internal Medicine, Head and Neck Surgery, and Division of Surgery, Houston; Reinhard Dummer, ProfDrMed, University Hospital Zürich, University Zürich; Nicholas A. Squittieri, MD, Li Liu, PhD, Sun Pharmaceutical Industries; Alexander Guminski, MD, PhD, Royal North Shore Hospital, University of Sydney; John Lear

Background: Sonidegib, a hedgehog pathway inhibitor, is approved in the US, EU, Switzerland, and Australia for locally advanced basal cell carcinoma (laBCC) not amenable to surgery or radiotherapy; and for metastatic BCC (mBCC) in Switzerland and Australia. We evaluated outcomes from the pivotal BOLT study per investigator or central review and corresponding concordance rates (CCR) for the approved 200-mg once-daily (qd) dose.

Methods: This phase 2, double-blind study, randomized laBCC or mBCC patients 1:2 to sonidegib 200 or 800 mg qd, respectively. Efficacy assessments included objective response rate (ORR), duration of response (DOR), and progression-free survival (PFS) per central and investigator review. Safety assessments included adverse event (AE) monitoring. Results At 42 months, ORR (95% confidence interval [CI]) in laBCC patients (n = 66) was 71.2% (58.7%-81.7%) vs 56.1% (43.3%-68.3%) per investigator vs central review (62%CCR). Per investigator vs central review, median DOR (95% CI) was 15.7 (12.0-20.2) vs 26.1 (not estimable [NE]) months and median PFS (95% CI) was 20.1 (14.8-23.8) vs 22.1 (NE) months. Patients with mBCC (n = 13) achieved ORR (95% CI) of 23.1% (5.0%-53.8%) vs 7.7% (0.2%-36.0%) per investigator vs central review (54%CCR). Per investigator vs central review, median DOR (95% CI) was 18.1 (17.7-18.4) vs 26.1 (NE) months and median (95% CI) PFS was 13.1 (9.2-19.4) vs 13.1 (5.6-33.1) months. AEs were mostly grade 1-2 and reversible with dose interruptions.

Conclusions: Despite differences in individual assessments, outcomes per investigator and central review support the efficacy of sonidegib in laBCC and mBCC.

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**Body surface area involvement with brodalumab in patients with moderate to severe plaque psoriasis**

April Armstrong, MD, MPH, University of Southern California; Benjamin D. Ehst, MD, PhD, Oregon Medical Research Center; Clive Liu, Abby Jacobson

Background: The percentage of affected body surface area (BSA) can be used to monitor psoriasis disease activity, with a, BSA of 3%-10% indicating a moderate disease state and >10% indicating a severe disease state. The fully human anti−interleukin-17 receptor A monoclonal antibody brodalumab is efficacious for the treatment of adults with moderate to severe plaque psoriasis. This post hoc analysis evaluates change in, BSA involvement over 52 weeks of treatment with brodalumab in a randomized phase 3 trial (AMAGINE-1).

Methods: In the 12-week induction phase, patients were randomized to brodalumab 210 mg every 2 weeks (q2w) or placebo. Thereafter, a subset of patients with a robust initial response (static Physician's Global Assessment score 0 or 1) remained on brodalumab 210 mg q2w for up to 52 weeks. Efficacy was monitored by percentage BSA involvement from baseline up to 52 weeks, reported using multiple imputation (induction phase) and last observation carried forward (rerandomization phase) analyses.

Results: Patients were initially randomized to receive brodalumab 210 mg q2w (n = 222) or placebo (n = 220). At baseline, mean (SD) percentage BSA involvement was 25.06 (15.25) in the brodalumab group and 26.90 (17.11) in the placebo group. After 12 weeks, percentage BSA involvement was significantly lower in patients treated with brodalumab (5.39 [11.86]) compared with placebo (29.80 [20.20]; least squares mean treatment difference vs placebo, −23.56; $P < .001$). Of patients who continued to receive brodalumab for 52 weeks (n = 83), percentage BSA involvement was 1.12 (4.65).

Conclusions: Continuous treatment with brodalumab for 52 weeks significantly decreased BSA involvement.

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**Pooled long-term safety analysis of risankizumab in patients with moderate to severe psoriasis**

Kenneth B. Gordon, MD, Department of Dermatology, Medical College of Wisconsin; Hervé Bachelez, MD, PhD, APHP Hopital Saint-Louis, Paris, France; Andrew Blauvelt, MD, MBA, Oregon Medical Research Center; Bruce Strober, MD, PhD, Yale University, New Haven, Connecticut, and Central Connecticut Dermatology Research, Cromwell; Stephanie Harbers, PhD, Joaquin Valdes, Brian Waterhouse, MS, Ranjeeta Sinvhal, Abbvie; Mark Lebwohl, MD, Icahn School of Medicine at Mount Sinai; Kristian Reich, MD, PhD, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf

Objective: Report short- and long-term risankizumab safety in patients with moderate to severe psoriasis.

Methods: Risankizumab safety was evaluated through week 16 (5 phase 2-3 trials, 150 mg vs adalimumab, ustekinumab, and placebo) and long-term (11 trials, all-risankizumab population, data cutoff March 29, 2019).

Results: Through week 16, adverse events (AEs) occurred in 48.9% (638/1306), 56.9% (173/304), 52.3% (125/239), and 48.3% (145/300) of patients receiving risankizumab 150 mg, adalimumab, ustekinumab, and placebo, respectively; serious AEs (SAEs) were 2.4%, 3.0%, 5.0%, and 4.0%. AEs were generally comparable across treatments and most were mild to moderate in severity. In the all-risankizumab population (n = 2673; 5582.8 patient years [PY]), the SAE rate remained consistent through week 16 (9.9/100PY) and long-term (8.6/100PY). Infection (90.8/100PY through week 16; 61.8/100PY long-term) and serious infection rates (1.7/100PY and 1.4 E/100PY) did not increase over time; the most common infections and serious infections with risankizumab were nasopharyngitis and upper respiratory tract infection and sepsis and pneumonia, respectively; there were no cases of active tuberculosis. Nonmelanoma skin cancer (NMSC, 0.7/100PY through week 16; 0.7 E/100PY long-term), malignant tumors excluding NMSC (0.7/100PY and 0.6 E/100PY), and major adverse cardiac event rates (0.2/100PY and 0.4/100PY) were similar through week 16 and long-term.

Conclusions: Risankizumab week-16 AE rates were low and similar to comparators and long-term risankizumab AE rates. These pooled safety data encompassing 5582.8 PY of exposure represent the largest and longest safety reporting so far with risankizumab and show that risankizumab treatment is safe and well tolerated in patients with moderate to severe psoriasis.

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**Duration of response and progression-free survival with sonidegib 200 mg once daily until disease progression or start of new antineoplastic therapy in patients with locally advanced basal cell carcinoma**

Michael Migden, MD, University of Texas, MD Anderson Cancer Center, Department of Dermatology, Division of Internal Medicine, Head and Neck Surgery, Division of Surgery, Houston; John Lear, Nicholas A. Squittieri, MD, Li Liu, PhD, Sun Pharmaceutical Industries; Alexander Guminski, Royal North Shore Hospital; Reinhard Dummer, ProfDrMed, University Hospital Zürich, University Zürich

Background: Sonidegib, a hedgehog pathway inhibitor, is approved in the US, EU, Switzerland, and Australia for locally advanced basal cell carcinoma (laBCC) not amenable to curative surgery or radiotherapy. This sensitivity analysis from the pivotal BOLT study presents duration of response (DOR) and progression-free survival (PFS), with start of new anticancer therapy considered progressive disease (PD), in aggressive and nonaggressive laBCC.

Methods: In this phase 2 double-blind study, laBCC or mBCC patients were randomized 1:2 to sonidegib 200 or 800 mg once-daily (qd), respectively. Tumor assessments used modified Response Evaluation Criteria in Solid Tumors for laBCC. Safety assessments included adverse event (AE) monitoring.

Results: At 42 months, ORR (95% confidence interval [CI]) in laBCC patients receiving the approved 200-mg qd dose (n = 66) was 56.1% (43.3%-68.3%), with median DOR (95% CI) of 26.1 months (not estimable [NE]) and median PFS (95% CI) of 22.1 months (NE). When considering new anticancer therapy as PD, median DOR (95% CI) in laBCC patients was 13.0 months (NE), while median PFS (95% CI) was 19.0 (14.0-30.7) months. In this sensitivity analysis, patients with aggressive laBCC (n = 37) achieved median DOR (95% CI) of 13.0 (7.4-35.7) months and median (95% CI) PFS of 14.9 (13.2-30.7) months. For nonaggressive laBCC (n = 29), median DOR was NE, while median PFS (95% CI) was 22.1 months (NE). AEs were mostly grade 1-2 and reversible with dose interruptions.

Conclusions: LaBCC patients receiving sonidegib 200 mg QD experienced durable tumor response until disease progression/start of new antineoplastic therapy.

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