INTRODUCTION: Pruritus (itch) is a frequent and vexing symptom of PBC that affects a majority of patients during the course of their disease. We now report the effect of seladelpar treatment over one year (1yr) on key patient reported measures of pruritus and quality of life (QoL).

METHODS: PBC patients with an inadequate response or intolerance to ursodeoxycholic acid (alkaline phosphatase ≥ 1.67 x upper limit of normal) were randomized to either seladelpar 2 mg, 5/10 mg (initial 5 mg with an option to adjust to 10 mg) or 10 mg groups (with no placebo) and treated for 1yr. Pruritus and QoL measures were evaluated at baseline (BL) through 1yr using visual analogue scale (VAS: 0-100), 5D-itch scale (5 domains: 1-5 each) and PBC-40 questionnaires.

RESULTS: Of 119 patients randomized to 2, 5 or 10 mg, we analyzed the 5/10 (n = 49) and 10 mg (n = 52) groups. Correlations (p < 0.0001) between different pruritus and QoL measures were noted: VAS vs 5-D itch (r = 0.83), VAS vs PBC-40 itch (r = 0.75) and VAS vs PBC-40 fatigue (r = 0.33). Significant correlations were observed between the changes in these pruritus measures after 1yr of treatment. Substantial improvement in pruritus (VAS ≥ 20-point decrease) at 1yr in patients with moderate to severe pruritus (VAS ≥ 40 at BL) was seen in 58% and 93% of patients in the 5/10 mg and 10 mg groups, respectively (Figure 1A). Improvement at 1yr in patients with moderate to severe BL itch by the 5-D itch score was seen in 62% (5/10 mg) and 82% (10 mg) of patients. Most frequent itching locations at BL were back, head/scalp, upper arms and forearms. The number of itching locations per patient (median [IQR]) decreased with seladelpar treatment after 1yr: 5/10 mg from 3 [0.5-8] to 2 [0-4]; 10 mg from 5 [1-9] to 1 [0-5]. About half of the patients experienced BL sleep disturbance due to itch as measured by the 5-D itch score. Of these patients, improvement in sleep disturbance at 1yr was observed in 81% (5/10 mg) and 78% (10 mg) of patients (Figure 1B). A consistent pattern of improvements in PBC-40 itch, sleep and fatigue were noted.

CONCLUSIONS: In patients with PBC treated with seladelpar for 1 year, improvements were observed in pruritus and sleep disturbance compared to baseline. The anti-pruritic effects of seladelpar are currently being evaluated in the placebo-controlled phase 3 ENHANCE study in PBC patients.
Figure 1. A. Changes in pruritus severity by VAS B. Changes in 5-D Itch sleep score in patients with baseline sleep disturbance due to itch.

Disclosure: A. E. Kremer: Abbvie: Speaking and Teaching; Beiersdorf: Advisory Committees or Review Panels; CMS: Speaking and Teaching; CymaBay: Advisory Committees or Review Panels; Eisai: Speaking and Teaching; Falk: Speaking and Teaching; Gilead: Speaking and Teaching; GSK: Advisory Committees or Review Panels; Intercept Pharmaceuticals: Grant/Research Support, Advisory Committees or Review Panels; MSD: Speaking and Teaching; Zambon: Speaking and Teaching; M. J. Mayo: Cara: Advisory Committees or Review Panels; CymaBay: Advisory Committees or Review Panels, Grant/Research Support; GSK: Advisory Committees or Review Panels, Grant/Research Support; Intercept: Grant/Research Support; Mallinckrodt: Grant/Research Support; Regeneron: Advisory Committees or Review Panels; Salix: Grant/Research Support; Target: Grant/Research Support; Target Pharmaceuticals: Advisory Committees or Review Panels; C. L. Bowius: BiomX: Consulting; CymaBay: Consulting; Gilead: Consulting; GSK: Consulting; Shire: Consulting; Trevi: Consulting; G. Neff: CLDF: Speaking and Teaching; Intercept: Speaking and Teaching; Mallinckrodt Pharm: Advisory Committees or Review Panels; M. G. Swain: Abbott: Speaking and Teaching; CymaBay: Advisory Committees or Review Panels, Grant/Research Support; Genkyotex: Grant/Research Support; Gilead: Advisory Committees or Review Panels, Speaking and Teaching, Grant/Research Support; GSK: Grant/Research Support; Intercept: Advisory Committees or Review Panels, Grant/Research Support; Novartis: Advisory Committees or Review Panels; M. Galambos: No Answer; A. Goel: No Conflicts; P. Trivedi: No Answer; G. Hirschfield: CymaBay: Consulting; GSK: Consulting; Intercept: Consulting; Roche: Consulting; Takeda: Consulting; R. Aspinall: Falk Pharma UK: Advisory Committees or Review Panels; Norgine UK: Speaking and Teaching; Sequana Medical: Speaking and Teaching; S. C. Gordon: No Conflicts; B. B. Borg: Cymabay: Grant/Research Support; S. Harrison: No Answer; P. Thuluvath: No Conflicts; D. E. Jones: Abbott: Speaking and Teaching; Falk: Speaking and Teaching; GSK: Consulting; Intercept: Speaking and Teaching, Grant/Research Support, Consulting; Pfizer: Grant/Research Support; Roche: Consulting; Y. Doerffel: No Conflicts; C. Levy: Cara Therapeutics: Advisory Committees or Review Panels, Grant/Research Support; CymaBay: Advisory Committees or Review Panels, Grant/Research Support; Durect: Grant/Research Support; Enanta: Grant/Research Support; Flashlight Therapeutics: Consulting; Genfit: Grant/Research Support; Genkyotex: Grant/Research Support; Gilead: Grant/Research Support; GSK: Advisory Committees or Review Panels, Grant/Research Support; HighTide: Grant/Research Support; Intercept: Grant/Research Support; NGM: Grant/Research Support; Novartis: Grant/Research Support; Pliant: Consulting; Shire: Advisory Committees or Review Panels; Target PharmaSolutions:
Grant/Research Support, Advisory Committees or Review Panels; Up-to-Date: Advisory Committees or Review Panels; C. Stanca: Cymabay: Grant/Research Support; D. Sheridan: No Conflicts; J. M. Vierling: Allergan: Grant/Research Support; Arena: Consulting; Enanta: Grant/Research Support; Genkyotex: Grant/Research Support; Gilead: Advisory Committees or Review Panels, Grant/Research Support; Intercept: Advisory Committees or Review Panels, Grant/Research Support; Lilly: Advisory Committees or Review Panels, Grant/Research Support; NGM Pharmaceuticals: Grant/Research Support; Novartis: Advisory Committees or Review Panels; M. L. Shiffman: Abbvie: Speaking and Teaching, Advisory Committees or Review Panels; Affimune: Grant/Research Support; Bayer: Advisory Committees or Review Panels; BMS: Advisory Committees or Review Panels, Speaking and Teaching; Celgene: Grant/Research Support; COnatus: Grant/Research Support; CymaBay: Grant/Research Support; Dova: Grant/Research Support, Advisory Committees or Review Panels, Speaking and Teaching; Eisai: Advisory Committees or Review Panels, Speaking and Teaching; Enanta: Grant/Research Support; Galmed: Grant/Research Support; genfit: Grant/Research Support; Gilead: Speaking and Teaching, Grant/Research Support, Advisory Committees or Review Panels; HepQuant: Advisory Committees or Review Panels; Intercept: Advisory Committees or Review Panels, Speaking and Teaching; Merck: Board Membership, Grant/Research Support, Speaking and Teaching; Valeant/Salix: Speaking and Teaching; T. Hassanein: AbbVie, Allergan, Assembly, BeiGene, Boehringer-Ingelheim, Bristol-Myers Squibb, Cymabay, Dova, Eisai, Enanta, Genetech, GenFit, Gilead, Grifols, Intercept, Mallinckrodt, Medicinova, Merck, Novartis, Obalon, Synlogic, Sundise, Salix, Shire, Valeant, Vital Therapies: Grant/Research Support; AbbVie, Baxter, Bristol-Myers Squibb, Dova, Gilead, Merck, Salix: Advisory Committees or Review Panels; D. Thorburn: No Conflicts; C. Berg: No Conflicts; D. Bernstein: Abbvie: Consulting, Intercept: Consulting; Mallinckrodt: Consulting; A. Gulamhusein: Abbvie: Speaking and Teaching; Intercept Pharmaceuticals: Speaking and Teaching; C. Landis: No Conflicts; A. Peyton: ABBVIE: Advisory Committees or Review Panels, Speaking and Teaching; GILEAD: Advisory Committees or Review Panels, Speaking and Teaching; INTERCEPT: Speaking and Teaching; SHINOGI: Speaking and Teaching; VALEANT: Speaking and Teaching; L. Corless: No Conflicts; P. Buggisch: Abbvie: Advisory Committees or Review Panels; Falk: Speaking and Teaching; Gilead: Advisory Committees or Review Panels; Intercept: Advisory Committees or Review Panels; MSD: Advisory Committees or Review Panels; Norgine: Speaking and Teaching; M. Wörns: abbvie: Advisory Committees or Review Panels; Bayer: Advisory Committees or Review Panels; BMS: Advisory Committees or Review Panels; Celgene: Speaking and Teaching; Eisai: Advisory Committees or Review Panels; Gilead: Speaking and Teaching; Incyte: Speaking and Teaching; Ipsen: Advisory Committees or Review Panels; Janssen: Speaking and Teaching; MSD: Speaking and Teaching; Roche: Advisory Committees or Review Panels; S. Berghaeunu: Cymabay Therapeutics: Consulting; M. Varga: No Conflicts; Y. Li: Cymabay Therapeutics, Inc: Employment; K. Yang: Cymabay Therapeutics: Employment; K. Dickinson: Cymabay Therapeutics Inc.: Employment; P. Boudes: No Conflicts; C. A. McWherter: No Answer; A. Steinberg: Cymabay Therapeutics: Employment; Y. Choi: Cymabay Therapeutics: Employment;