Update of SEL-212 Phase 2 Clinical Data in Symptomatic Gout Patients: SVP-Rapamycin Combined with Pegadricase Mitigates Immunogenicity and Enables Sustained Reduction of Serum Uric Acid Levels, Low Rate of Gout Flares and Monthly Dosing

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Abstract

Background/Purpose: Pegylated uricases are promising therapies for the treatment of severe chronic gout, but are limited by their immunogenicity. We have previously shown that synthetic vaccine particles encapsulating rapamycin (SVP-Rapamycin) co-administered with pegadricase (formerly known as pegsiticase) prevented the formation of anti-drug antibodies (ADAs) in a dose-dependent manner. A Phase 1b study of SEL-212, a novel combination product candidate consisting of pegadricase and SVP-Rapamycin, demonstrated sustained control of serum uric acid (SUA) for at least 30 days after a single dose. Here we report data on the safety, tolerability, and effects on SUA, ADAs, and gout flares of five monthly doses of SEL-212 in symptomatic gout patients treated with 0.1 or 0.15 mg/kg SVP-Rapamycin in combination with 0.2 mg/kg pegadricase.

Methods: Patients with symptomatic gout (≥1 tophus, gout flare within 6 months, and/or gouty arthropathy) and elevated SUA (≥6 mg/dL) were enrolled in SEL-212 treatment cohorts. Patients reported here received up to five monthly doses of SEL-212 (0.2 mg/kg pegadricase combined with 0.1 or 0.15 mg/kg SVP-Rapamycin). Safety, tolerability, SUA, and ADAs were monitored, and clinical data were collected.

Results: As of 09 Oct 2018, 152 patients had been dosed in the Phase 2 study. All evaluable patients receiving 0.1 or 0.15 mg/kg SVP-Rapamycin administered with 0.2 mg/kg pegadricase who achieved three months of SUA control maintained SUA control in months four and five of combination treatment. Projection for remaining patients in 5 dose cohorts suggest approximately 66% of patients will maintain SUA levels below 6 mg/dL at week 20 after five monthly doses of SEL-212. The sustained reduction of SUA correlated with low or no ADAs. SEL-212 was generally well tolerated and associated with a low rate of gout flare rates. Thirty-five percent of patients treated with five doses of 0.1-0.15 mg/kg SVP-Rapamycin, and only 29% of all current patients in the SEL-212 Phase 2 trial, experienced gout flares after initiation during the first month of treatment with continued reduction of gout flare rates over months two through five. This low rate of gout flares appears to be in contrast with higher incidence of gout flares reported in clinical trials involving other urate lowering therapies.

Conclusion: SEL-212 has been well-tolerated, showing substantially reduced immunogenicity, sustained control of SUA, and low rate of gout flares with repeated monthly dosing.

Disclosures

ES, WD, LJ, and TKK are employees and shareholders of Selecta Biosciences

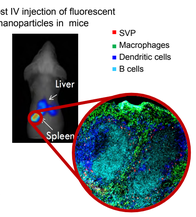
Background

Pegadricase

Pegadricase

- Uricases have been shown to be very effective in significantly reducing serum uric acid levels in patients with chronic severe gout
- Uricases are highly immunogenic, compromising their safety and efficacy
- Pegadricase is a pegylated uricase enzyme that is being developed in combination with SVP-Rapamycin to mitigate its immunogenicity

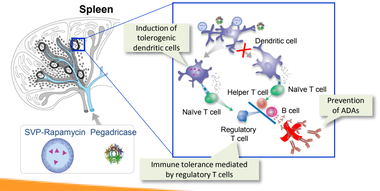
SVP-Rapamycin



- SVP-Rapamycin is a biodegradable nanoparticle that encapsulates rapamycin, an mTOR inhibitor
- Intravenous injection of SVP-Rapamycin results in selective accumulation in the spleen and liver, where it is endocytosed by dendritic cells (DC) and macrophages
- SVP-Rapamycin is designed to be co-administered with biologic drugs to mitigate the formation of ADAs through the induction of immune tolerance and thus enable sustained therapeutic activity of the biologic (Kishimoto et al., 2016, Nature Nanotech)

SEL-212

- SEL-212 is a combination drug comprised of pegadricase and SVP-Rapamycin
- The co-administration of SVP-Rapamycin and pegadricase is designed to induce the formation of regulatory T cells that mitigate the formation of ADAs against pegadricase and enable sustained reduction of serum uric acid (sUA) levels



Results

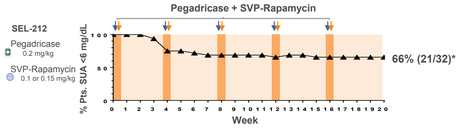
SEL-212/201: Ongoing Phase 2 Clinical Trial

Study description

- Evaluate the safety, pharmacokinetics, pharmacodynamics and immunogenicity of repeated monthly IV infusions of SEL-212 in patients with symptomatic gout and elevated SUA levels (>6 mg/dL)
- Cohorts of patients administered five q28 day IV infusions of 0.2 mg/kg pegadricase in combination with 0.1 - 0.15 mg/kg doses of SVP-Rapamycin
- Monitored for safety, uric acid levels, uricase pharmacodynamic activity, and anti-uricase-antibodies (ADAs)
- Male or female subjects ages 21 to 75 inclusive

Clinicaltrials.gov NCT02959918

Patients (%) With Sustained SUA Control



Full 20 week data are pending for 5 patients in the 5 dose cohorts

- 16/16 patients (100%) who completed 20 weeks of combination treatment had SUA <6 mg/dL at 12 weeks and maintained control through 20 weeks
- The 5 patients who are pending had SUA <6 mg/dL at 12 weeks

*We project 66% of patients (21/32) will complete the 20 week period with SUA< 6 mg/dL based on rate of SUA control for patients who have completed the treatment period

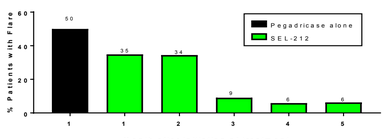
Week 20 Evaluable patients = patients who received a full first dose and did not discontinue due to any measure other than drug effectiveness or drug related safety

SEL-212 Five monthly dose cohorts

Cohort	Treatment Week 0		Treatment Weeks 4, 8, 12, 16		Status
	Pegadricase	SVP-Rapamycin	Pegadricase	SVP-Rapamycin	
13	0.2 mg/kg	0.15 mg/kg	0.2 mg/kg	0.15 mg/kg	Ongoing
15	0.2 mg/kg	0.15 mg/kg	0.2 mg/kg	0.1 mg/kg	Ongoing
17	0.2 mg/kg	0.1 mg/kg	0.2 mg/kg	0.1 mg/kg	Ongoing

- Five monthly dose cohorts demographics:
  - 46 patients with established or symptomatic gout (≥1 tophus, ≥ 1 gout flare in last 6 months, or chronic gouty arthropathy) with hyperuricemia (> 6mg/dL SUA)
  - Average SUA at enrollment/screening: 8.3 mg/d
  - Average age: 53.6 (range 23-70)
  - Male, 45 (97.8%); Female, 1 (2.2%)
  - Caucasian, 34 (73.9%); African American, 10 (21.7%); Asian 1 (2.2%) and Other 1 (2.2%)
  - Mean BMI at baseline: 34.5 kg/m^2 (71.7% of patients moderately obese)
  - Mean duration of established or symptomatic gout: 12.5 years.

Incidence of Gout Flares by Month



- Data indicate SEL-212 lowers flares initially and over time during treatment
- Majority of flares occur in months 1 & 2
- There are no new patients who flare after second month

Patients who received a full first dose and completed respective treatment cycle

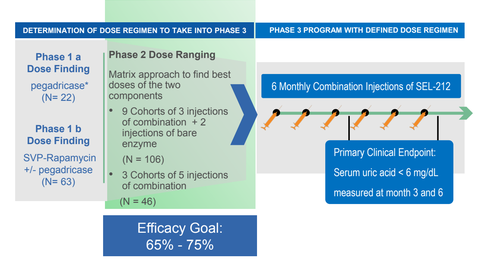
Safety

- SEL-212 has been generally well tolerated at clinically active doses for 5-combination dose cohorts following >130 administrations
- 46 patients in 5-combination dose cohorts have been dosed in the Phase 2 study as of October 9, 2018
- 5 months of combination treatment has not shown any emerging safety signals
- 7 SAEs (5 individual patients) reported in the 5-combination dose cohorts:
  - 4 SAEs were reported not to be or unlikely to be related to study drug
  - 1 SAE was reported to be possibly related to study drug
  - 2 SAEs (infusion reactions) were reported as related or possibly related to study drug, both of which occurred during the infusion of SEL-212 in Treatment Period 2
  - No SAEs occurred in Treatment Periods 4 or 5

Summary

- Projections suggest 66% of patients with SUA control during 5 months of treatment
- Monthly dosing
- Low flare rates
- DECT imaging shows potential to rapidly eliminate tissue urate burden (see poster 2205)
- 5 months combination treatment has not shown any emerging safety signals
- Proposed dose regimens identified for Phase 3 trials

SEL-212 Clinical Development Plan



Acknowledgements

We thank all of the patients that participated in the clinical trial. We are very grateful to the clinical trial site investigators, their staff and the entire Selecta SEL-212 project team

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