SEL-212 Phase 2 Clinical Data in Symptomatic Gout Patients: ImmTOR Tolerogenic Nanoparticles 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: Pegylated uricases are promising therapies for the treatment of severe chronic gout, but are limited by their immunogenicity. We have previously shown that ImmTOR tolerogenic nanoparticles (formerly known as SVP-Rapamycin) encapsulating rapamycin co-administered with pegadricase prevented the formation of anti-drug antibodies (ADAs) in a dose-dependent manner. A prior Phase 1b study of SEL-212, a novel combination product candidate consisting of pegadricase and ImmTOR, demonstrated sustained control of serum uric acid (SUA) for at least 30 days after a single dose. Here we provide data from a recently completed Phase 2 multidose clinical trial.

Objectives: To assess 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 ImmTOR 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 ImmTOR). Safety, tolerability, SUA, and ADAs were monitored, and clinical data were collected.

Results: As of 17 Dec 2018, 152 patients had been dosed in the Phase 2 study. All evaluable patients receiving 0.1 or 0.15 mg/kg ImmTOR 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. Approximately 66% of evaluable patients maintained 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. Only 35% of patients treated with five doses of 0.1-0.15 mg/kg ImmTOR, and 29% of all 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. SEL-212 has a favorable product profile to address the unmet need of patients with severe, chronic gout including low immunogenicity allowing continued dosing, lower reported flare rates and convenient monthly dosing.

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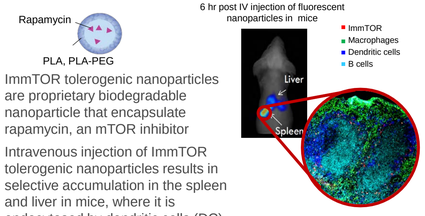
Background

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 proprietary pegylated uricase enzyme that is being developed in combination with ImmTOR tolerogenic nanoparticles to mitigate its immunogenicity

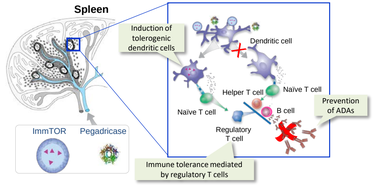
ImmTOR Tolerogenic Nanoparticles



- ImmTOR tolerogenic nanoparticles are proprietary biodegradable nanoparticle that encapsulate rapamycin, an mTOR inhibitor
- Intravenous injection of ImmTOR tolerogenic nanoparticles results in selective accumulation in the spleen and liver in mice, where it is endocytosed by dendritic cells (DC) and macrophages
- ImmTOR tolerogenic nanoparticles are 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 ImmTOR tolerogenic nanoparticles
- The co-administration of ImmTOR tolerogenic nanoparticles 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

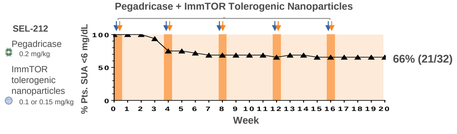
SEL-212/201: Phase 2 Clinical Trial

Study description

- 32 out of 46 patients were evaluable for efficacy (male and female subjects ages 23 to 66)
- Study objectives were to 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 were administered five q28 day IV infusions of 0.2 mg/kg pegadricase in combination with 0.1 - 0.15 mg/kg doses of ImmTOR tolerogenic nanoparticles
- Patients were monitored for safety, uric acid levels, uricase pharmacodynamic activity, and anti-uricase-antibodies (ADAs)

Clinicaltrials.gov NCT02959918

Patients (%) With Sustained SUA Control



- 66% of evaluable patients (21/32) maintained SUA levels below 6 mg/dL at week 20 after 5 monthly doses of SEL-212
- 100% of patients (21/21) who had SUA <6 mg/dL at 12 weeks maintained control through 20 weeks
- Sustained reduction of SUA levels correlated with low or no ADAs

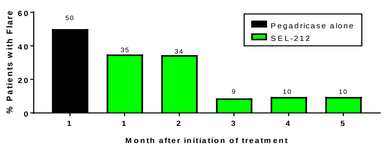
Week 20 Evaluable patients = patients who received a full first dose and did not discontinue due to any measure other than drug effectiveness or drug related safety

Dose Cohorts

Cohort	Treatment Week 0		Treatment Weeks 4, 8, 12, 16	
	Pegadricase	ImmTOR	Pegadricase	ImmTOR
A	0.2 mg/kg	0.15 mg/kg	0.2 mg/kg	0.15 mg/kg
B	0.2 mg/kg	0.15 mg/kg	0.2 mg/kg	0.1 mg/kg
C	0.2 mg/kg	0.1 mg/kg	0.2 mg/kg	0.1 mg/kg

- 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/dL
  - 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 compared to historical pegadricase alone data
- Majority of flares occur in months 1 & 2
- There were no patients with initial flares after second month

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

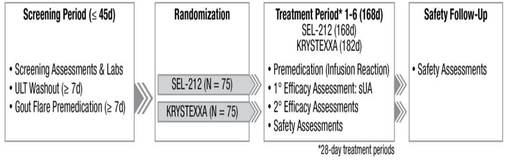
Safety

- SEL-212 was generally well tolerated at clinically active doses for 5-combination dose cohorts after 143 administrations in 46 patients
- The five monthly dosing regimen showed no new or emerging safety signals compared to earlier cohorts treated with three monthly doses
- 9 SAEs (6 individual patients) reported in dose cohorts:
  - 7 SAEs were reported not to be or unlikely to be related to study drug
  - 2 SAEs (infusion reactions) were reported as related or possibly related to study drug, both of which occurred during the second infusion of SEL-212 (pegadricase)

Summary

- 66% of patients maintained SUA control during 5 months of treatment with monthly combination dosing (ImmTOR tolerogenic nanoparticles + pegadricase)
- Sustained reduction of SUA levels correlated with low or no ADAs
- Low flare rates throughout the study
- 5 months of combination treatment did not show-any emerging safety signals
- Dose regimen identified for COMPARE clinical trial (SEL-212 vs KRYSTEXXA®)

SEL-212/202 COMPARE Study Design



Acknowledgements

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Disclosures

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