

Initial Phase 2 Clinical Data of SEL-212 in Symptomatic Gout Patients: Measurement of Dissolution of Urate Deposits Associated with Monthly Dosing of a Pegylated Uricase (Pegadricase) with SVP-Rapamycin By Dual Energy Computed Tomography

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Abstract

Background: Pegylated uricases are therapies for treatment of severe chronic gout, particularly for rapid resolution of tophi. However, uricases are limited by induction of anti-drug antibodies (ADAs) that can compromise efficacy and safety. SEL-212 is a novel combination product candidate consisting of pegadricase (formerly known as pegsiticase) co-administered with synthetic vaccine particles encapsulating rapamycin (SVP-Rapamycin). We report initial Phase 2 data on the effect of the intensive lowering of serum uric acid (SUA) levels by SEL-212 on the dissolution of monosodium urate (MSU) crystals in symptomatic gout patients.

Dual-energy computed tomography (DECT) may be used to differentiate urate crystals from calcium by using specific attenuation characteristics, to diagnose gout. DECT uses a computer algorithm to produce color-coded images that render uric acid green, cortical bone blue, and trabecular bone purple. In tophaceous gout patients, DECT may be used for serial volumetric quantification of subclinical tophi to evaluate response to treatment.

Methods: Patients with symptomatic gout (≥1 tophus, gout flare within 6 months or gouty arthropathy) and elevated SUA ≥6 mg/dL were treated with monthly doses of pegadricase (0.2 mg/kg or 0.4 mg/kg) alone or in combination with SVP-Rapamycin (0.05 to 0.15 mg/kg). SEL-212 was infused in 28-day cycles x3 doses followed by challenge with pegadricase alone on 28-day cycles x2 doses, or in 28-day cycles x5 combination doses of SVP-Rapamycin and pegadricase.

To investigate changes in uric acid deposits, DECT scans of hand/wrist, feet/ankles, and knees were performed as an exploratory measure in a subset of patients, during the screening visit, treatment period 3, treatment period 5 or at early termination visit. DECT images were analyzed by Arthritis Research Canada (ARC) by two DECT Radiologists utilizing a Syngo Via DECT software package

Results: As of 09 Oct 2018, an initial DECT scan was performed in a subset of 31 of 152 dosed patients, with 19 patients with an available follow-up DECT scan. The demographics for patients (N=19) who received a follow-up DECT scan were 43 - 71 years old (mean 55.4 years), male 89.5%, African American 47.4%, and Caucasian 52.6%. Mean BMI at baseline was 33.1 kg/m², with 63% of patients being obese. Mean duration of gout was 8.0 years.

The mean SUA at the screening visit was 7.9 mg/dL. Time between the initial and most recent/follow-up DECT scan ranged from 77 - 163 days (mean 121 days), with a mean change in total urate volume of -1.18 cm³ (range: 0.11 to -13.03 cm³).

Conclusion: SEL-212 has a significant impact on the reduction of urate deposits in symptomatic gout patients with hyperuricemia as confirmed by DECT.

DECT Imaging

- DECT (Dual Energy Computed Tomography) is a sensitive and non-invasive diagnostic tool to quantify tissue urate burden^{1,2}

¹Choi HK et al., Ann Rheum Dis. 2009, 68:1609-12.
²Araujo EG et al, RMD Open. 2015, 1:e000075.

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 pegylated uricase enzyme that is being developed in combination with SVP-Rapamycin to mitigate its immunogenicity

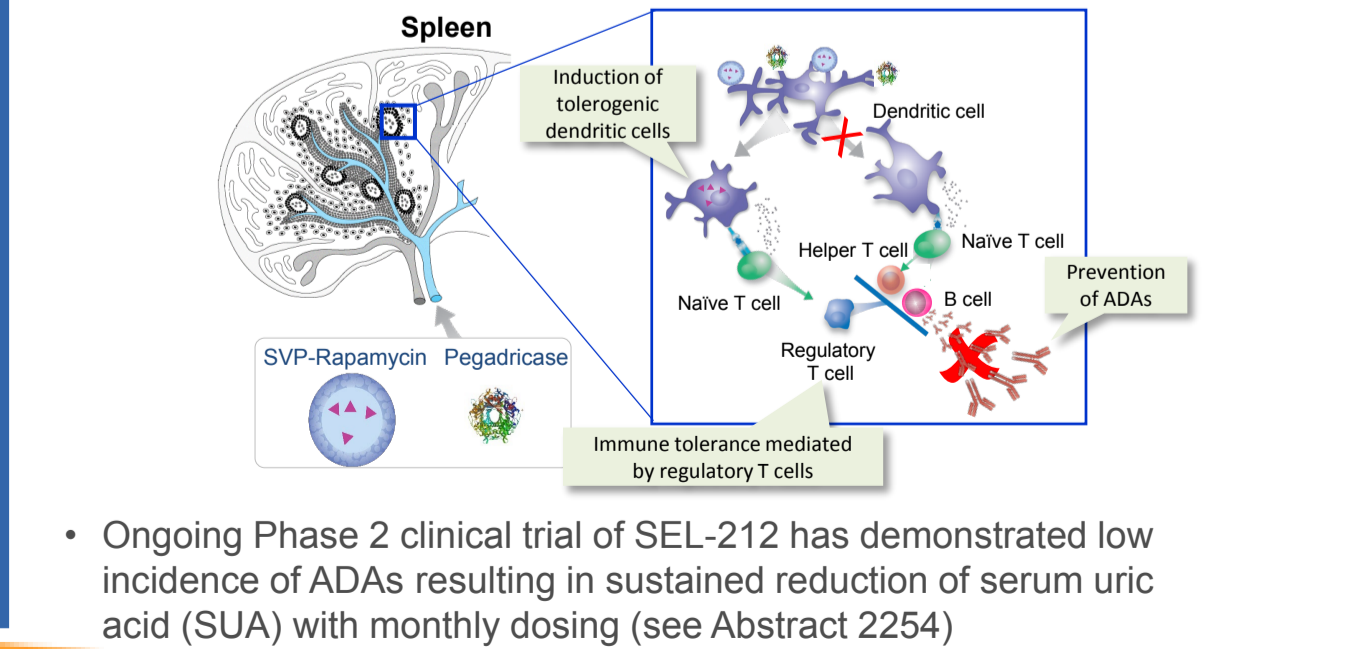
SVP-Rapamycin

6 hr post IV injection of fluorescent nanoparticles in mice

- 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 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 candidate 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

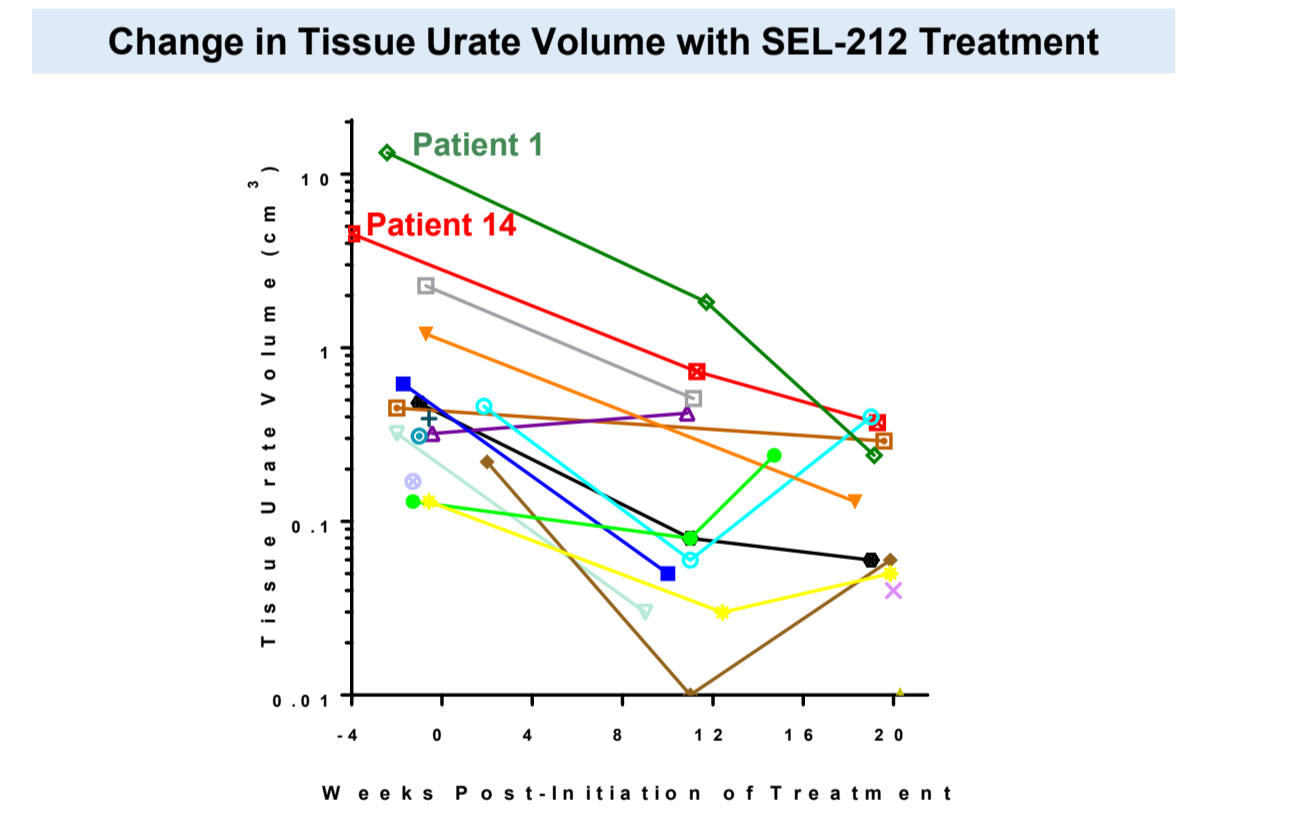
Overview of DECT Scans Performed in SEL-212/201 Study

To investigate changes to uric acid deposits, DECT scans were performed at the following timepoints as an exploratory measure

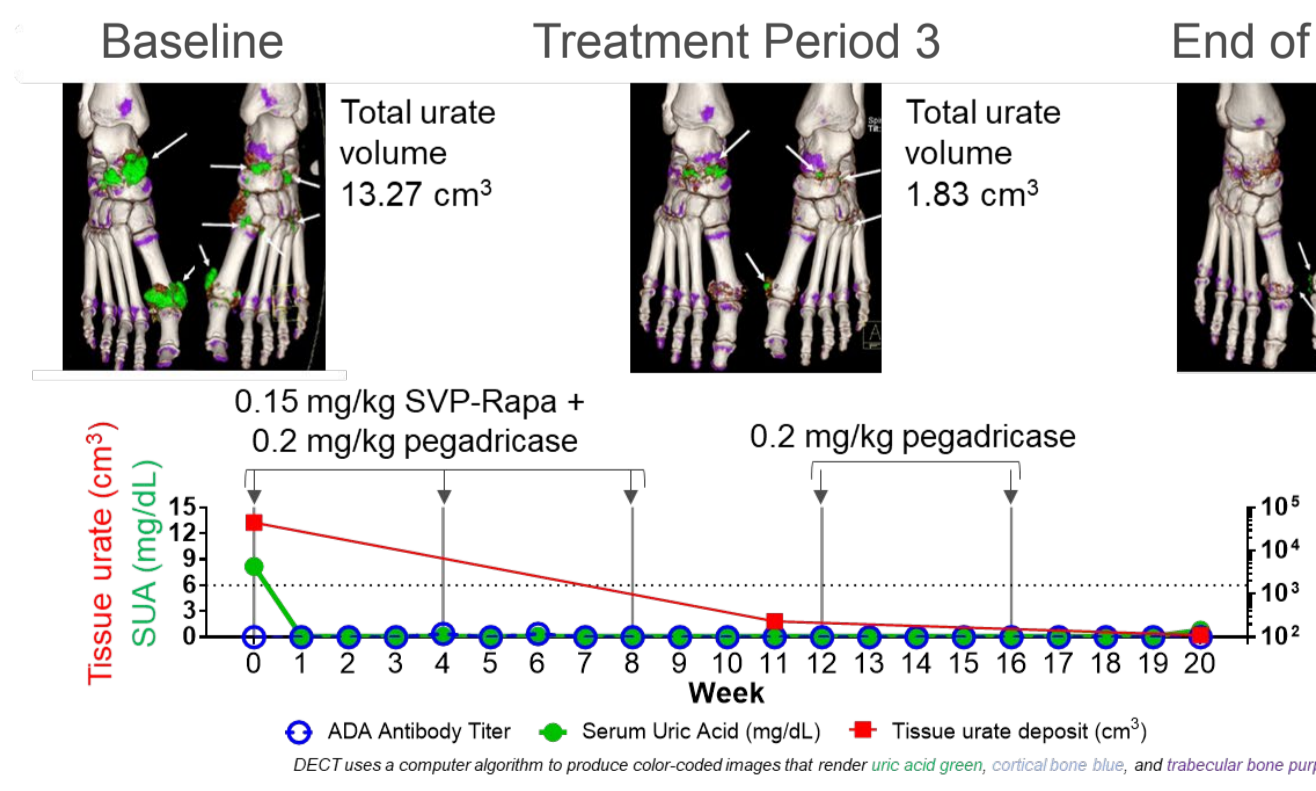
- Baseline
- After Treatment Period 3
- After Treatment Period 5 or at Early Termination Visit

Baseline DECT scan was performed in 31 dosed patients, with 19 patients undergoing a follow-up DECT scan as of 09 Oct 2018

- Demographics for Patients with Follow-Up DECT Scans
 - Average SUA at enrollment/screening: 7.9 mg/dL
 - Average age: 55.4 (range 43-71)
 - Male, 17 (89.5%)
 - Caucasian: 52.6%; African American: 47.4%
 - Mean BMI at baseline: 33.1 kg/m² (63.2% of patients were moderately obese)
 - Mean duration of established or symptomatic gout: 8 years



Patient 1 DECT Scan Images Show Significant Reduction of Tissue Urate Burden



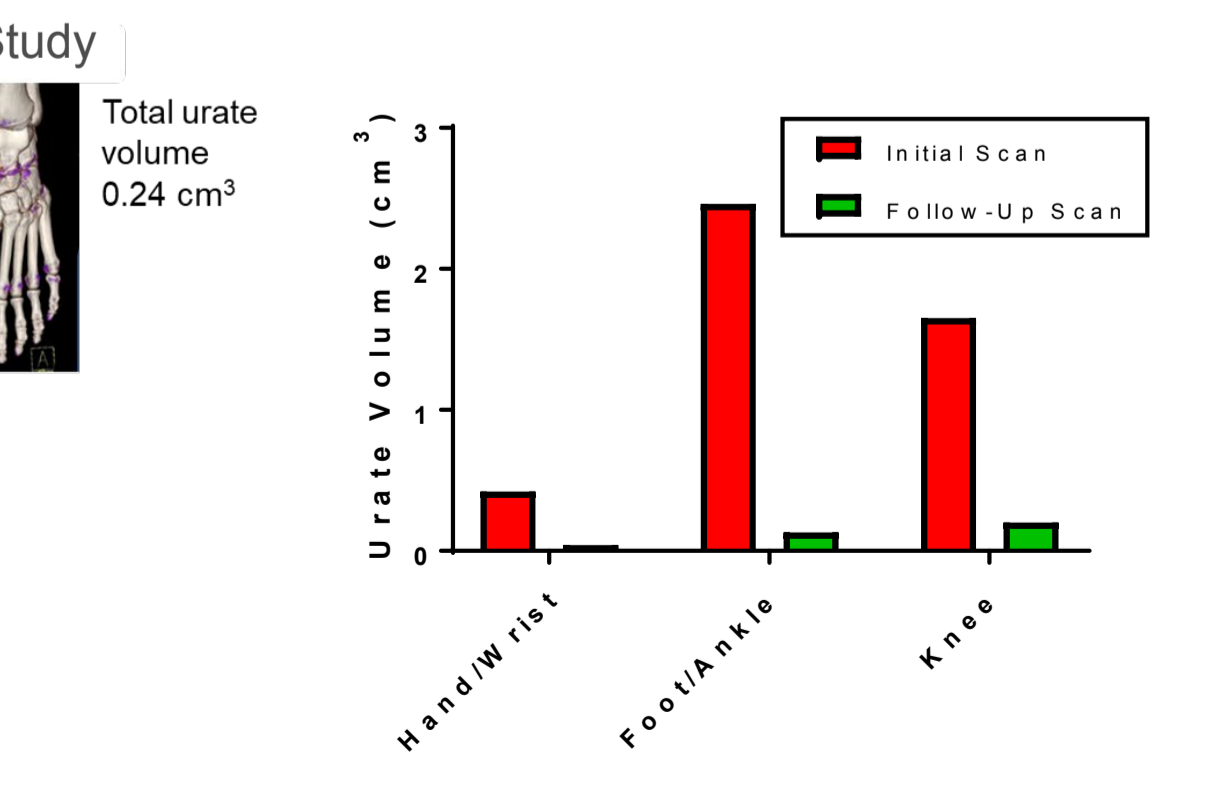
Total Urate Change in Patients with at Least One Follow Up Scan

Patient #	Baseline SUA (mg/dL)	Number of Study Drug Infusions	Initial Urate Volume (cm ³)	Final Urate Volume (cm ³)	Change in urate volume (%)
1	8.2	5	13.27	0.24	-98.19
2	6.3	3	0.13	0.24	84.62
3	8.5	2	0.62	0.05	-91.94
4	7.6	5	0.00	0.01	NA*
5	7.4	5	1.20	0.13	-89.17
6	8	5	0.39	0.00	-100.00
7	6.7	5	0.00	0.04	NA*
8	8.9	5	0.22	0.06	-72.73
9	7.7	5	0.46	0.40	-13.04
10	8.9	3	2.27	0.51	-77.53
11	8.8	5	0.32	0.42	31.25
12	11.1	2	0.32	0.03	-90.63
13	8.2	5	0.45	0.29	-35.56
14	6	5	4.53	0.37	-91.83
15	6.4	5	0.48	0.06	-87.50
16^	6.5	5	0.13	0.05	-61.54
17^	9.6	5	0.31	0.00	-100.00
18^	8.6	5	0.17	0.00	-100.00
19^	7.5	1	0.00	0.00	NA*

- Patients with available repeat scans are included in this summary
- For the 31 patients with baseline scans, the range of urate volume at baseline was 0.00 to 61.05 cm³
- For the 19 patients with repeat scans as of Oct 9 2018, the range of urate volume at baseline was 0.00 to 13.27 cm³
- Mean time between the initial and most recent/follow-up DECT scan: 121.2 days (ranged from 77 to 163 days)

*NA = Not Applicable, ^Patients in 5 combination dose cohorts

Patient 14: Before and After Treatment



Summary

- SEL-212 is a monthly combination product candidate being developed as a therapy for the sustained control of SUA leading to the removal of urate crystal deposits in patients with chronic severe gout
- SEL-212 has been well-tolerated, and, compared to pegylated uricase alone, has mitigated immunogenicity, reduced flare rates, and enabled repeated monthly dosing with sustained control of SUA levels
- SEL-212 has a significant impact on the reduction of urate deposits in symptomatic gout patients with hyperuricemia as confirmed by DECT
- Significant decrease in total urate deposits occurs progressively over the entire treatment period as observed by DECT

Acknowledgements

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Disclosures

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

