Summary of Data: Clinical

Three clinical studies in humans have been completed; one in 36 healthy male and female volunteers (GE-101-001), one in 30 elderly male and female volunteers (GE-101-003) and one in 31 subjects with prostate cancer (NCT1229618). All studies were conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP).

Study Title	Study No. Or Author(s)	Results Summary
A phase 1, placebo-controlled, randomised, ascending-dose study to assess the safety and tolerability of Pyruvate Injection in healthy male and female volunteers	GE-101-001	Doses of Pyruvate Injection up to 0.43 ml/kg were well tolerated in young, healthy male and female volunteers. Throughout the study, serum biochemistry, haematology, urinalysis, vital signs and ECG variables showed overall stability and no dose-related tendencies. No clinically important trends or safety signals were noted. The percentage of AEs attributed to IMP is higher in subjects given Pyruvate Injection than those given placebo, most of these events (e.g., flushing, dysgeusia and dizziness) were mild, short-lasting symptomatic reactions that are commonly reported after intravenous injection of 10 ml or more of other types of contrast agents, e.g., those used for X-ray and MRI examinations. Therefore, this difference does not raise any concerns.
A phase 1, placebo-controlled, randomised, ascending-dose study to assess the safety and tolerability of Pyruvate Injection in elderly male and female volunteers	GE-101-003	The most common AEs were headache, dysgeusia and diarrhoea, each experienced by 10% of the subjects who received Pyruvate Injection and none of the subjects who received placebo. Throughout the study, serum biochemistry, haematology, vital signs and ECG variables showed overall stability and no dose-related tendencies. No clinically important trends or safety signals were noted. The percentage of AEs attributed to IMP is higher in subjects given Pyruvate Injection than those given placebo, most of these events (e.g., dysgeusia, feeling hot, pharyngeal discomfort and flushing) were mild, short-lasting symptomatic reactions that are commonly reported after intravenous injection of 10 ml or more of other types of contrast agents, e.g., those used for X-ray and MRI examinations. Therefore, this difference does not raise any concerns.
Phase 1 ascending dose study in 31 subjects with prostate cancer access the safety and tolerability and imaging potential of hyperpolarized [1-13C] pyruvate Injection via 13C imaging (13C MRI) and 13C MR spectroscopic imaging (13C MRSI)	NCT01229618 (UCSF & GE)	Safety: In phase 1 of the study, dose escalation from 0.14 ml/kg to 0.43 ml/kg there were a total of 10 mild adverse events in eight of eighteen patients, classified as grade 1 by Common Terminology Criteria for Adverse Events (CTCAE) v4.0.criteria. The highest dose of [1-13C]pyruvate (0.43 ml/kg) was selected for further study on the basis of the higher signal-to-noise ratio (SNR) of hyperpolarized [1-13C]pyruvate that was observed. In phase 2, there were an additional 10 events observed in five of ten patients, but, , none were considered to be dose-limiting toxicities (DLTs). The single episode of dizziness that was seen in one patient during phase 2 was attributed to extra dosing of atenolol, which was used by the subject to reduce anxiety rather than the hyperpolarized agent. There was one episode of grade 2 diarrhea reported in the phase

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		2 component, which was attributed to an enema that the patient received. Expansion cohort: to optimize the imaging protocol and explore the biological variability in delivery, transport, and metabolism of the agent, 13 patients were imaged. Single–time point 2D or 3D acquisitions were used to obtain arrays of 13C spectra from the prostate and surrounding tissues in 8 to 12 s. The initial sequence parameters were chosen on the basis of studies in murine and dog models, but were further refined as the study progressed in terms of the start times for acquiring MR data and the flip angle schemes used