CT511 - A phase 1 trial of AMP945, a potent and selective focal adhesion kinase inhibitor, in healthy volunteers

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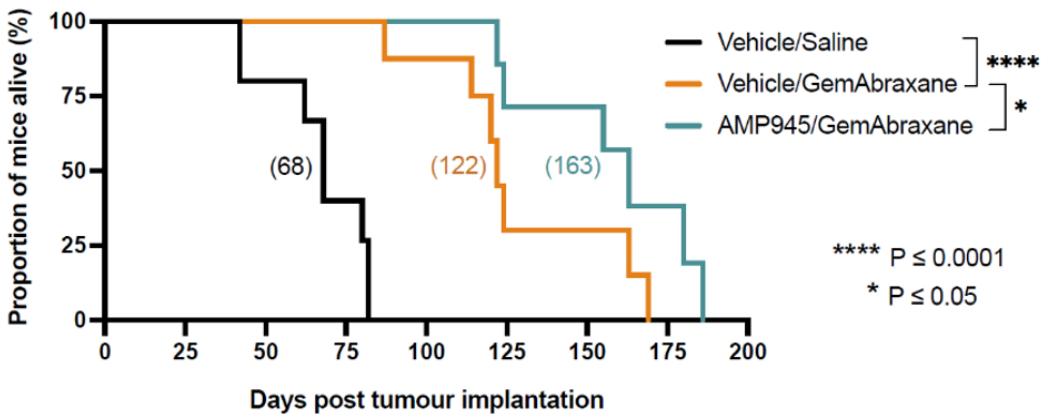
Exposing cancer. Enhancing treatment.

AMP945 - a highly potent and selective inhibitor of focal adhesion kinase (FAK)

- FAK is a non-receptor tyrosine kinase with key roles in a variety of cellular processes, in particular those related to the adhesion and migration of many cell types
- Multiple studies have shown FAK to be a key player in the establishment and maintenance of the tumour microenvironment
- AMP945 is a potent, orally bioavailable small molecule inhibitor of FAK
- Amplia is developing AMP945 in both oncology and fibrosis indications

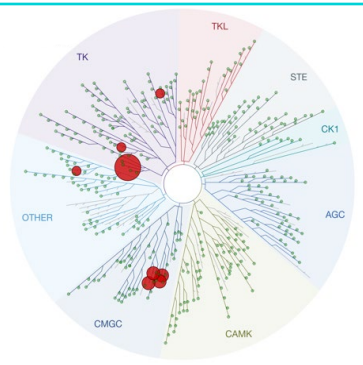
Pulsed dosing of oral AMP945 with nab-paclitaxel/gemcitabine enhances survival in the TKCC-10-LO Orthotopic Pancreatic Cancer Model*



* Data from Paul Timpson Laboratory, Garvan Institute of Medical Research

Preclinical safety assessment per ICH M3(R2) → **Phase 1 trial in healthy volunteers**

AMP945 Attributes	
FAK inhibition	IC_{50} 2.2 nM
Pyk2 inhibition	IC_{50} 550 nM
CYP inhibition	> 20 µM all isoforms
Glutathione trapping	negative
Kinase selectivity	Highly selective for FAK across 468 kinase screen

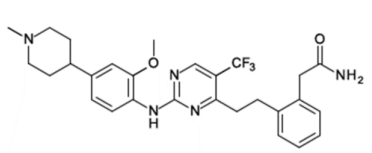


Selectivity score (S10) 0.02

Phase 1 trial design

Randomized, double-blinded, placebo-controlled in healthy volunteers (18 - 50 years)

AMP945



Single ascending dose (SAD)

Placebo

AMP945 *Fasted*

AMP945 *Fed*

n=2	15mg	n=6
n=2	30mg	n=6
n=2	60mg	n=6
n=2	125mg	n=6

Wash out period

Multiple ascending dose (MAD)

Placebo

AMP945 *7 Consecutive days*

n=2	25mg	n=6
n=2	50mg	n=6
n=2	100mg	n=6

Outcomes

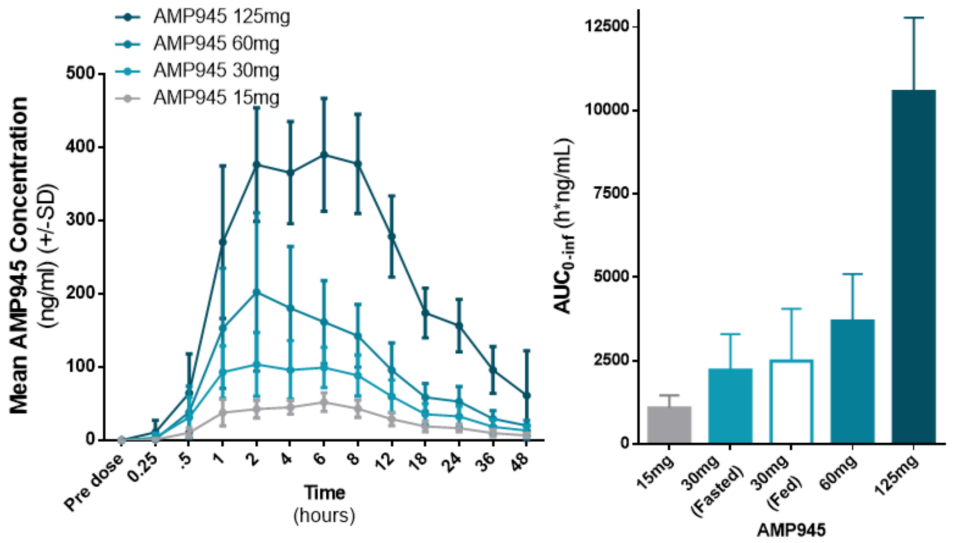
	Single ascending dose (SAD)	Multiple ascending dose (MAD)
Blood Collection Pharmacokinetic analyses	Pre-dose and 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24, 36, and 48 h post-dose	Pre-dose and 0.25, 0.5, 1, 2, 4, 6, 8, 12, 24 h post-dose on Days 1 and 7 Pre-dose on Days 2-6
Skin Biopsy Pharmacodynamic analyses	Before and after dosing with 125 mg	Before and after dosing with 25, 50, 100mg

Safety and tolerability were assessed according to incidence and severity of adverse events (AEs).

ANZCTR: ACTRN12620000894998

Results – plasma pharmacokinetics of AMP945

Single ascending dose (SAD)



- Food consumption did not result in a change of AMP945 pharmacokinetics.

- **Mean time to maximum plasma concentration:** 1 to 6 h

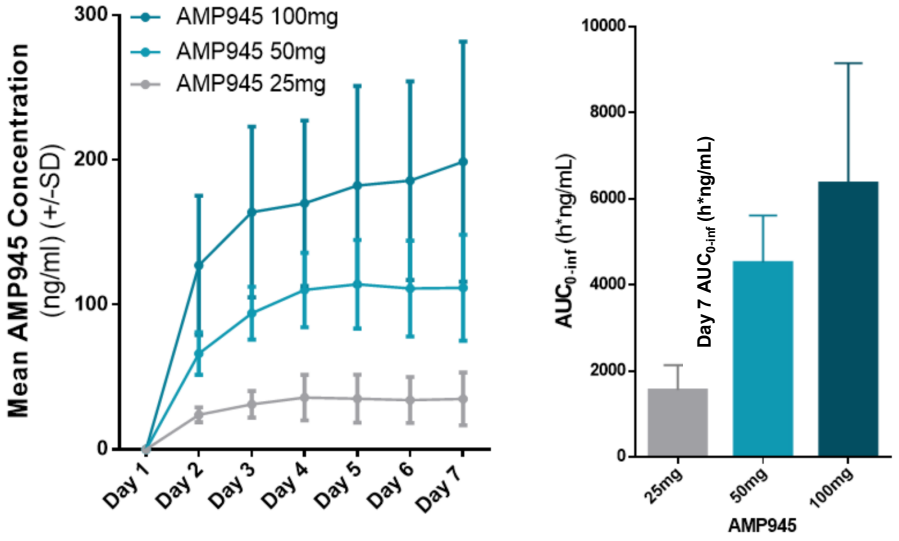
- **Median half-life** ranged from 15.7 to 23 h

→ Supports feasibility of QD dosing

- **Mean apparent volume of distribution** ranged from 328 to 463 L

→ Indicates tissue-wide distribution

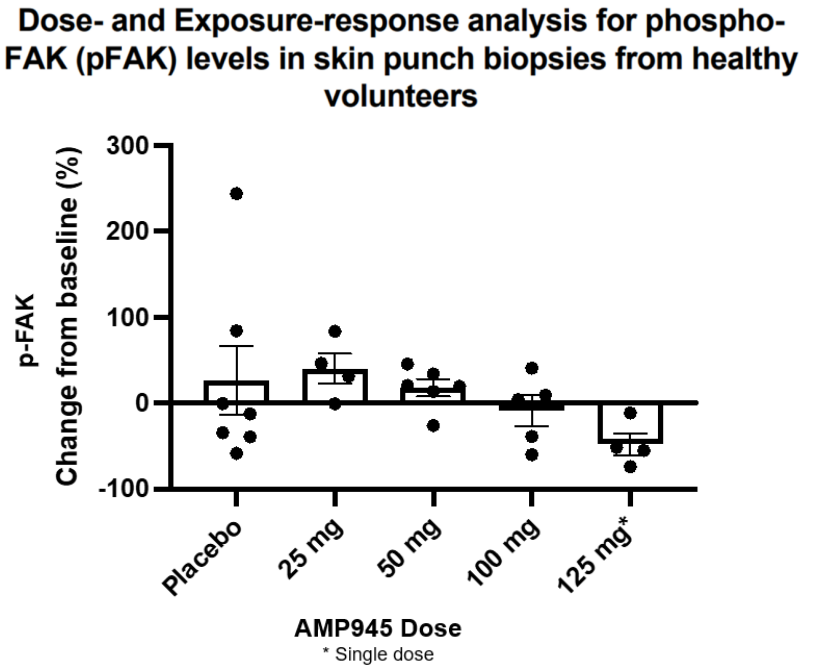
Multiple ascending dose (MAD)

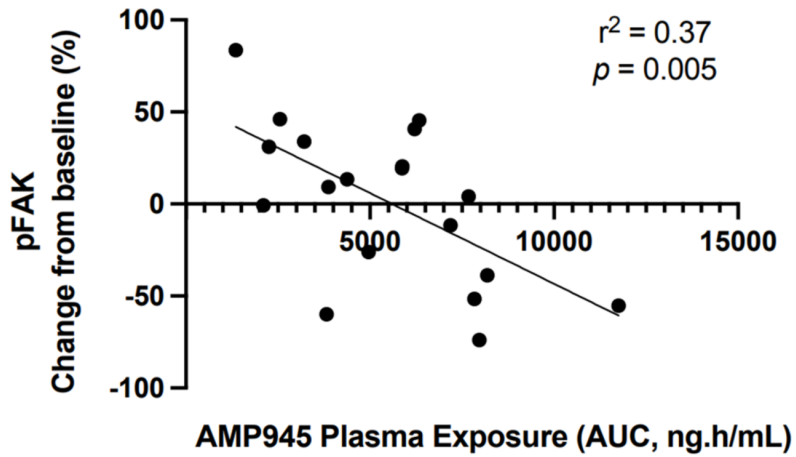


- **Mean time to maximum plasma concentration:** 2 to 4 h

- Observations of pre-dose trough levels between Day 1 and Day 7 indicated that steady state was achieved by Day 4 to Day 5 (approximately 5 x t1/2)

Results – Pharmacodynamics and safety





- Significant (linear) relationship observed between the change in FAK activity from baseline and AMP945 $AUC_{0\text{-inf}}$ following dosing with 25, 50, 100 and 125 mg of AMP945.

Safety Summary

- No serious or severe TEAEs, nor any TEAEs leading to study withdrawal (majority of TEAEs reported were mild)
- There were no dose-related trends observed in the reporting of TEAEs
- No TEAEs were considered probably or definitely related to AMP945:
- No changes over time or dose-related trends in clinical safety laboratory parameters;
- No changes over time or dose-related trends in vital signs, ECG, physical examination and concomitant medications reporting.

Conclusions - Phase 1 trial of AMP945

- AMP945, a selective FAK inhibitor, **was safe and well tolerated** across SAD (15 to 125 mg) and MAD (25 to 100 mg) cohorts in healthy volunteers.
  - No serious adverse events or withdrawals
  - No trends observed in AE reporting, no shifts in clinical laboratory, vital signs, ECGs.
- AMP945 PK and PD data demonstrate **wide tissue distribution and target engagement.**
  - Predictable dose/exposure relationship
  - Evidence of pharmacodynamic effect in skin punch biopsies
- The data supports continued development of AMP945 in patients with solid tumours and fibrotic diseases in which FAK inhibition would be beneficial

Thank you – john@ampliatx.com