Savolitinib clinical trials
June 2016 update

List of abbreviations

BID	Twice Daily
CRC	Colorectal Cancer
DoR	Duration of Response
EGFRm	Epidermal Growth Factor Receptor mutation
EGFRwt	Epidermal Growth Factor Receptor wild type
FISH	Fluorescence In Situ Hybridization testing
FPD	First Patient Dosed
IHC	Immunohistochemistry testing
LPCD	Last Patient Commenced Dosing

MET	Aberation of c-Met/HGF
MTD	Maximum Tolerated Dose
NSCLC	Non-Small Cell Lung Cancer
ORR	Overall Response Rate
OS	Overall Survival
PFS	Progression Free Survival
QD	Once Daily
RCC	Renal Cell Carcinoma
TKI	Tyrosine Kinase Inhibitor

Savolitinib (AZD6094*; Highly selective MET TKI)

Non-small cell lung cancer (NSCLC)

Study phase	Patient population	Number of patients	Design	Endpoints	Status
Phase I/II **TATTON** **NCT02143466**	Advanced EGFRm NSCLC TKI failure	Phase Ib N = 18 Phase II expansion N ~ 25	Phase Ib – 3 dose-finding arms 1. Combination Tagrisso + savolitinib (AZD6094, MET inhibitor) Phase IIa/IIb open label combination • Combination Tagrisso 80mg + savolitinib 600mg Global trial	Phase Ib • Safety, tolerability, pharmacokinetics • Preliminary anti-tumour activity Phase IIa/IIb • Objective Response Rate (ORR) • Secondary endpoints include duration of response, PFS and OS	• FPD: Q3 2014 • Dose escalation completed • FPD: Q3 2015 • LPCD: Q4 2016
	Advanced EGFRm NSCLC TKI failure, with primary resistance mutation T790M and subsequent resistance to T790M TKI	N ~ 20	• Tagrisso + savolitinib • T790M mutation positive patients that failed on Tagrisso or other T790M TKI • MET-driven resistance patients Global trial	Phase II • ORR • Secondary endpoints include duration of response, PFS and OS	• FPD: Q1 2016 • LPCD: 2017
Phase I/II **NCT02374645**	Advanced EGFRm NSCLC TKI failure	Phase Ib N = 12 Phase II expansion N = 40	Phase Ib • Open label, dose finding study • Combination Iressa + savolitinib Phase II expansions • Combination Iressa 250mg + savolitinib 600mg • Screening for MET gene amplified patients Conducted in China	Phase Ib • Safety and tolerability Phase II expansions • ORR • Secondary endpoints include duration of response, PFS and OS	Phase Ib • FPD: Q1 15 • LPCD: Q2 15 Phase II expansions • FPD: Q3 15 • LPCD Q4 16
Phase I/II **NCT01985555**	3rd line Advanced EGFRwt NSCLC	N = 22	• Savolitinib monotherapy • MET IHC or FISH positive patients Conducted in China	• Safety, tolerability and pharmacokinetics • Preliminary anti-tumour activity	• FPD: Q4 14 • LPCD: Q4 15 • Completed (not yet published)
	Advanced EGFRwt NSCLC	N = 10	• Savolitinib monotherapy • All lines • Exon 14 deletion mutation patients Conducted in China	• Safety, tolerability and pharmacokinetics • Preliminary anti-tumour activity	• FPD: Q3 16 • LPCD: Q4 17

*Also known as HMPL-504; formerly known as volitinib

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Renal cell carcinoma (RCC)

Study phase	Patient population	Number of patients	Design	Endpoints	Status
Phase II **NCT02127710**	Papillary RCC	N = 109	Single arm, open label study • savolitinib 600mg QD • MET status of all patients fully assessed Conducted in UK, Spain, US, Canada	• Objective Response Rate (ORR) • Secondary endpoints include duration of response, PFS and OS	• FPD: Q2 14 • LPCD: Q4 15 • Est. top-line results: Q4 16
Phase II **NCI PAPMET** **NCT02761057**	Metastatic papillary RCC	N = 180	Randomized, efficacy assessment of multiple MET kinase inhibitors vs. sunitinib 1. sunitinib 2. cabozantinib 3. crizotinib 4. savolitinib Conducted in 78 locations in the US Sponsored by the National Cancer Institute (NCI)	• PFS, ORR, OS, safety & tolerability	• FPD: Q2 16 • Est. completion: Q1 19
Phase Ib **CALYPSO**	Metastatic papillary RCC	N ~ 40	Part 1: Dose-finding study of durvalumab + savolitinib Part 2: durvalumab + savolitinib combination expansion Conducted in UK Sponsored by Queen Mary University of London	• Efficacy, biomarker analysis, MTD	• FPD: Q2 16 • Est. Completion: Q4 19
	Metastatic clear cell RCC	N ~ 40	VEGFR TKI refractory patients • Savolitinib 600mg QD Conducted in UK Sponsored by Queen Mary University of London	• Efficacy, biomarker analysis, MTD	• FPD: Q2 16 • Est. Completion: Q4 19
	Metastatic clear cell RCC	N ~ 40	VEGFR TKI refractory patients • Part 1: Dose-finding study of durvalumab + savolitinib • Part 2: durvalumab + savolitinib combination expansion Conducted in UK Sponsored by Queen Mary University of London	• Efficacy, biomarker analysis, MTD	• FPD: Q2 16 • Est. Completion: Q4 19

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Gastric cancer

Study phase	Patient population	Number of patients	Design	Endpoints	Status
Phase I/II **NCT01985555**	Advanced gastric cancer	N = 10	• Savolitinib monotherapy • MET gene amplified patients • All lines Conducted in China	• Safety, tolerability and pharmacokinetics • Efficacy – PFS	• FPD: Q4 14 • LPCD:Q4 17
	Advanced gastric cancer	N = 24	• Savolitinib monotherapy • MET overexpression patients • Third line Conducted in China	• Safety, tolerability and pharmacokinetics • Efficacy – PFS	• FPD: Q4 14 • LPCD: Q4,15
Phase Ib **NCT02252913**	Advanced Gastric Adenocarcinoma	N = 4	• Dose finding – combination docetaxel + savolitinib • Second-line MET gene amplified patients Conducted in China	• Safety, tolerability and pharmacokinetics	• FPD: Q4 14 • Completed (not yet published)
	Advanced Gastric Adenocarcinoma	N = 4	• Dose finding – combination docetaxel + savolitinib • Second-line MET overexpression patients Conducted in China	• Safety, tolerability and pharmacokinetics	• FPD: Q4 14 • Completed (not yet published)
Phase Ib/II VIKTORY **NCT02447406** **NCT02447380** **NCT02449551**	Advanced Gastric Adenocarcinoma	N = 25	• Combination docetaxel + savolitinib • Second-line MET gene amplified patients Conducted in South Korea Sponsored by Samsung Medical Center	• Safety, tolerability and pharmacokinetics • Efficacy – ORR, PFS, DoR, OS	• FPD: Q1 15 • Est. completion: Q4 18
	Advanced Gastric Adenocarcinoma	N = 25	• Combination docetaxel + savolitinib • Second-line MET overexpression patients Conducted in South Korea Sponsored by Samsung Medical Center	• Safety, tolerability and pharmacokinetics • Efficacy – ORR, PFS, DoR, OS	• FPD: Q3 15 • Est. completion: Q1 18
	Advanced Gastric Adenocarcinoma	N = 20	• Savolitinib monotherapy • Third-line MET gene amplified patients Conducted in South Korea Sponsored by Samsung Medical Center	• Safety, tolerability and pharmacokinetics • Efficacy – ORR, PFS, DoR, OS	• FPD: Q1 15 • Est. completion: Q1 18

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Other cancer studies

Study phase	Patient population	Number of patients	Design	Endpoints	Status
Phase I **NCT01773018**	Advanced Solid Tumors	N = 50 Expansion N = 10	• First dose escalation study • QD & BID • Expansion into PRCC and cetuximab failure CRC patients Conducted in Australia	• Safety, tolerability and pharmacokinetics • Preliminary activity	• FPD: Q1 12 • Completed
Phase I **NCT01985555**	Advanced Solid Tumors	N = 70	• Phase I dose escalation study Conducted in China	• Safety, tolerability and pharmacokinetics • Preliminary activity	• FPD: Q2 13 • Completed

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