MIV-818 phase Ia results

JUNE 13, 2019

MEDIVIR

SCIENCE WORKING WONDERS

Introduction

HCC is the third leading cause of cancer-related deaths worldwide

- Estimated new cases 2018: Asia: ~ 610,000; US: ~ 42,000; EU: ~ 82,000
- Orphan disease in Western markets, but one of fastest growing and most deadly cancers in US
- High incidence in Asia including China - Hepatitis B & C very common
- Five-year survival: 18%
- Genetically heterogeneous leading to limited effect of molecularly targeted therapies

MIV-818 for treatment of liver cancer

- MIV-818 is a proprietary new chemical entity discovered at Medivir
- MIV-818 is being developed as a new treatment for HCC and other liver cancers as a stand alone treatment or in combination with standard of care

Patients with advanced liver cancer are in need of new therapies

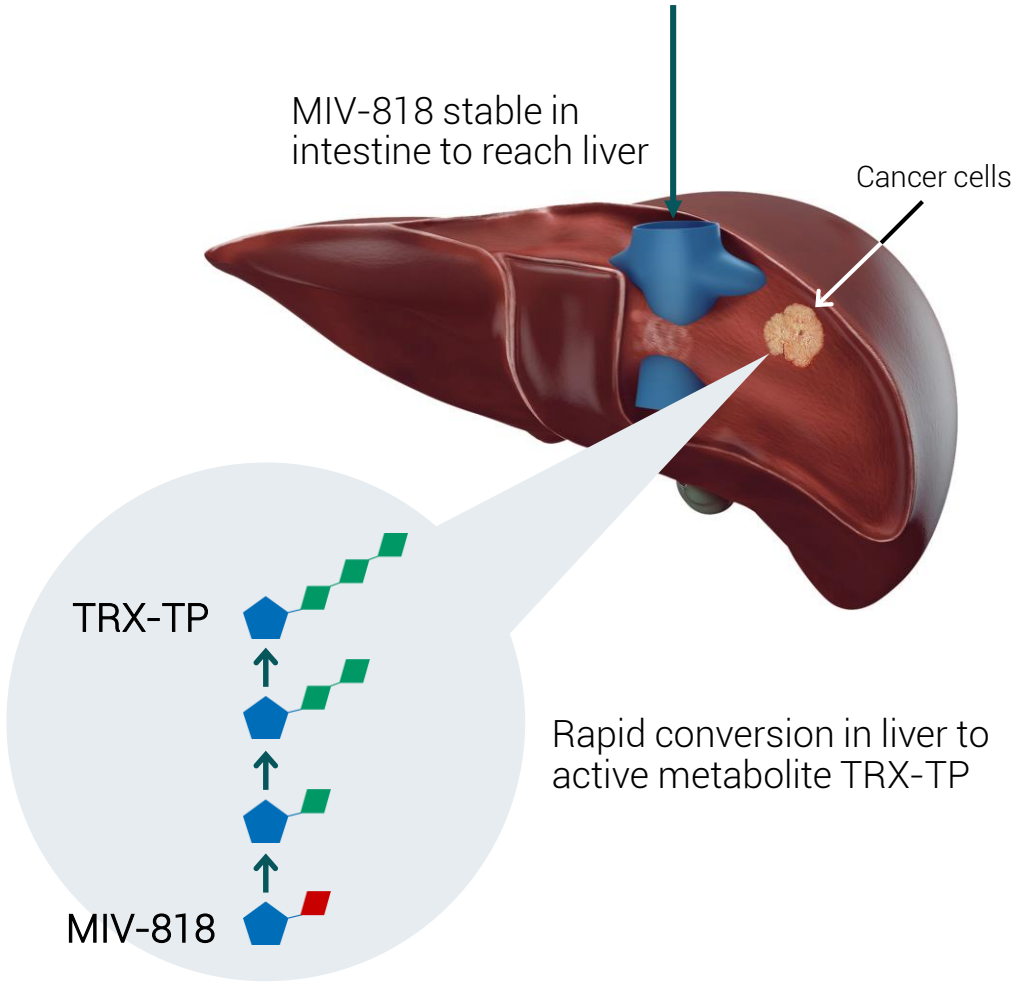
Mechanism of Action

Chain-terminating inhibition of DNA synthesis

- MIV-818 is an orally administered nucleotide prodrug of the active metabolite troxacitabine triphosphate (TRX-TP)
- When incorporated into DNA, TRX-TP causes double strand DNA breaks and cell death
- Troxacitabine progressed to Phase 2/3, with clinical responses observed in several cancers, but development halted due to the narrow therapeutic window

Liver targeting to deliver high levels of the active metabolite to the liver while minimizing exposure elsewhere

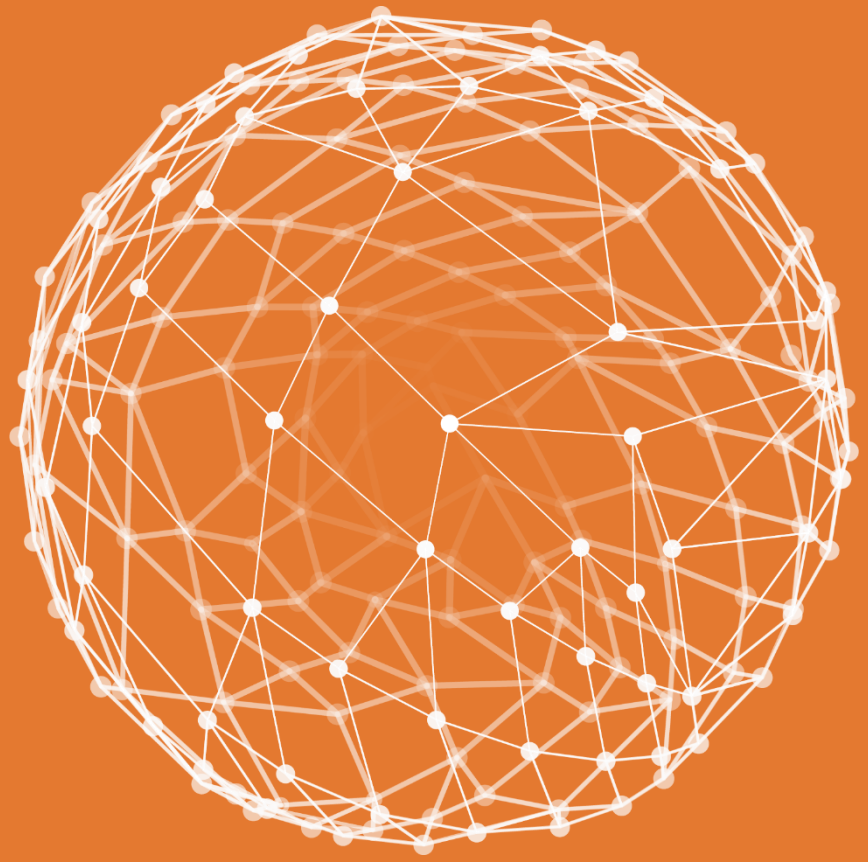
- MIV-818 has been designed to minimize systemic exposure and limit the toxicity of troxacitabine by primarily targeting the liver
- This prodrug technology has been clinically proven to deliver high liver levels of nucleotides in patients with compensated cirrhosis[1]



[1]Babusis et al., Antimicrob Agents Chemother. 2018, doi: 10.1128/AAC.02587-17

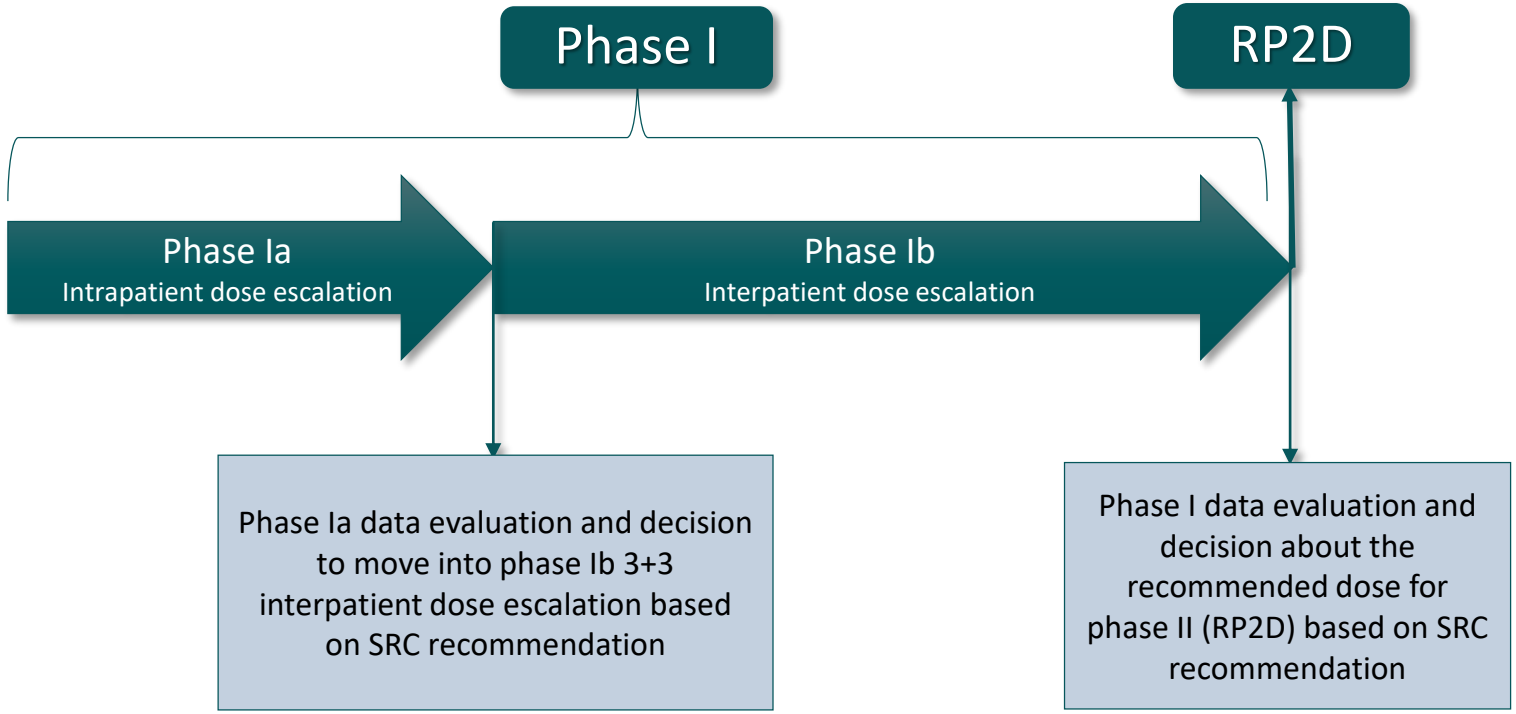
MEDIVIR

MIV-818 phase I study design



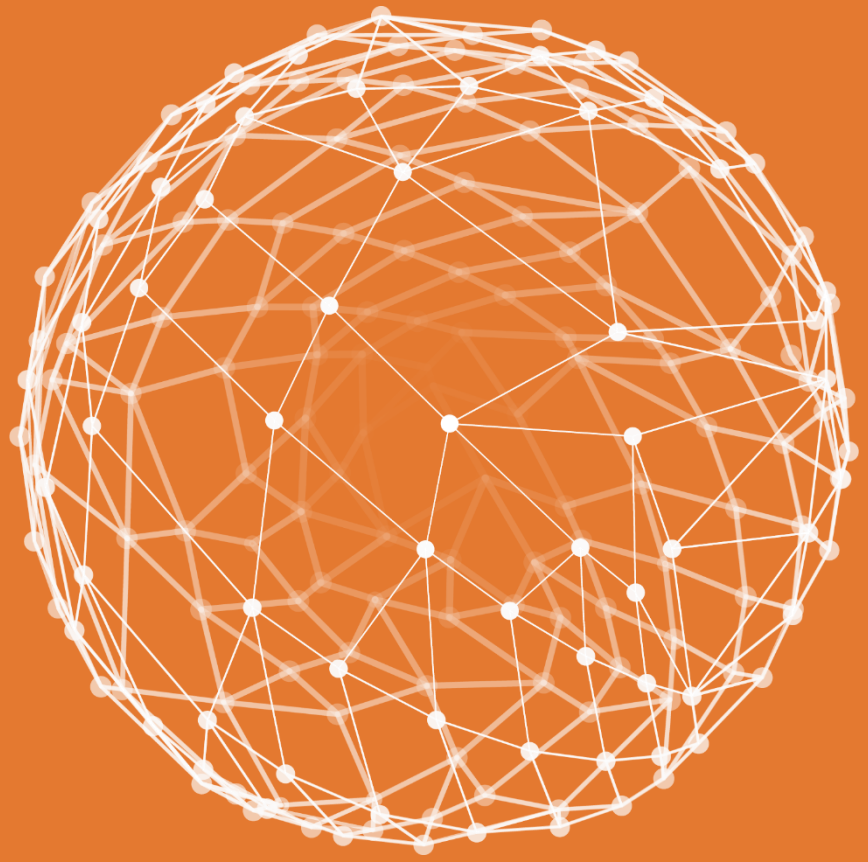
MEDIVIR

Phase I - study design



MEDIVIR

Phase Ia summary preliminary results



MEDIVIR

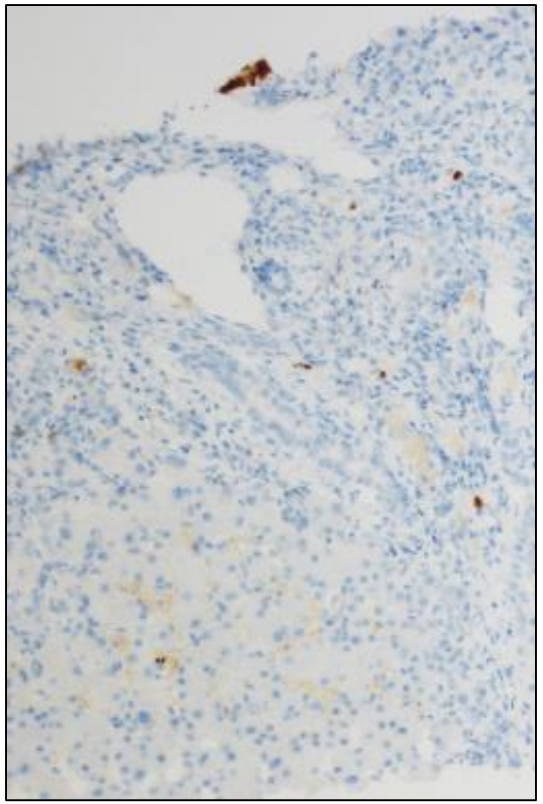
Phase Ia - preliminary safety data

- The primary aim of the phase Ia study is to evaluate the safety and tolerability of MIV-818
- In addition, exploratory objectives include pharmacokinetics and biomarkers of activity
- Data is available from the first 6 patients in the study
- The patients included have advanced liver cancer i.e. hepatocellular carcinoma, intrahepatic cholangiocarcinoma and liver metastatic disease
- The patients have been treated with escalating doses of orally administered MIV-818
- MIV-818 has in general been well tolerated. Lowering of blood counts for Patient 6 and platelet count for Patient 5 after 4 cycles suggest we are now seeing impact from dosing and are close to a maximum tolerated dose of MIV-818

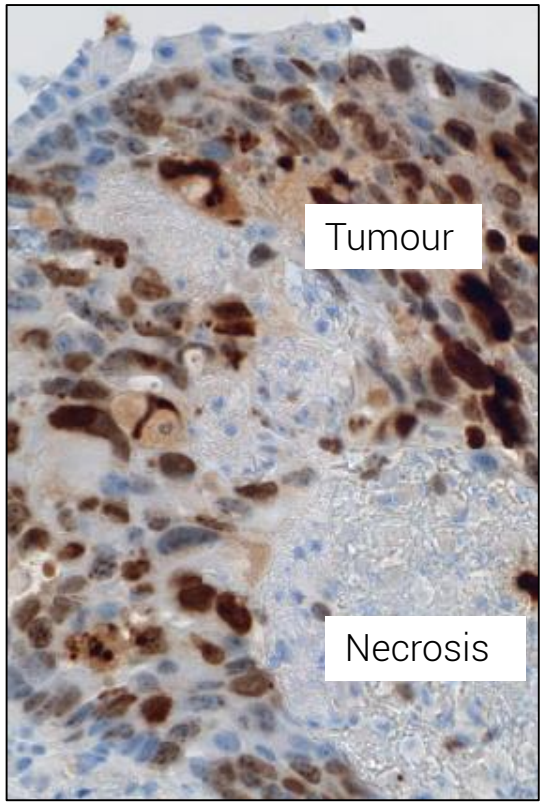
MIV-818 induces DNA-damage response in liver tumour tissue

Clear evidence of pH2AX induction (brown nuclear stain) resulting from DNA-damage in tumour but not normal liver tissue

Normal liver

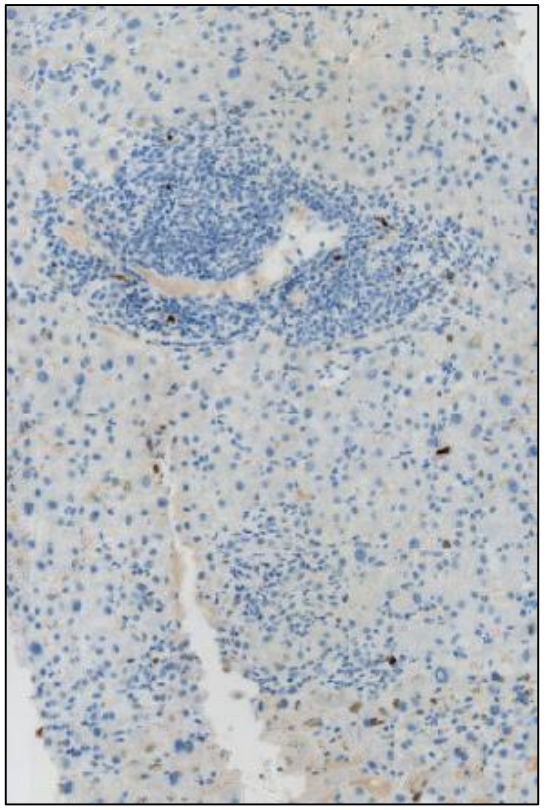


Tumour tissue

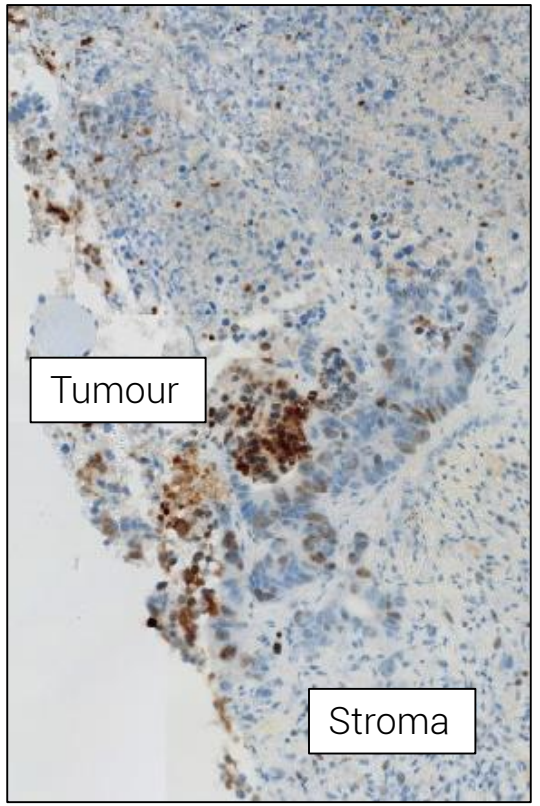


Data from Patient 2

Normal liver



Tumour tissue



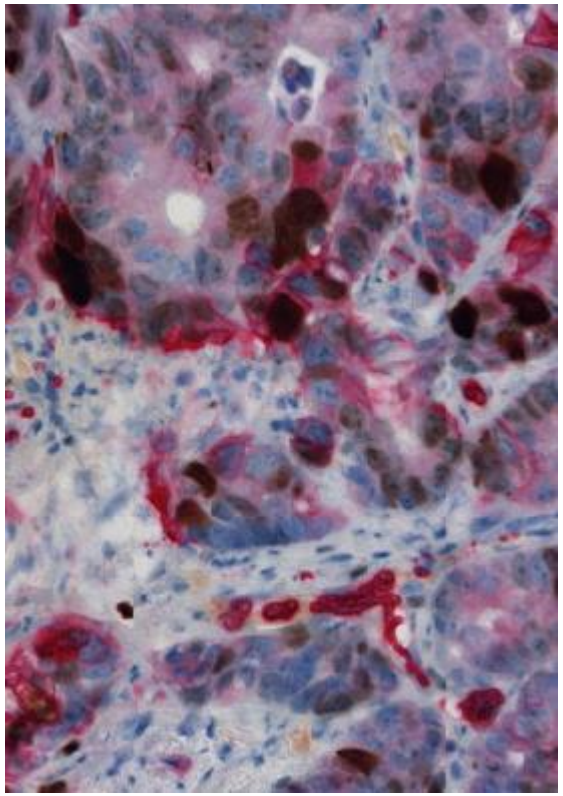
Data from Patient 4

MEDIVIR

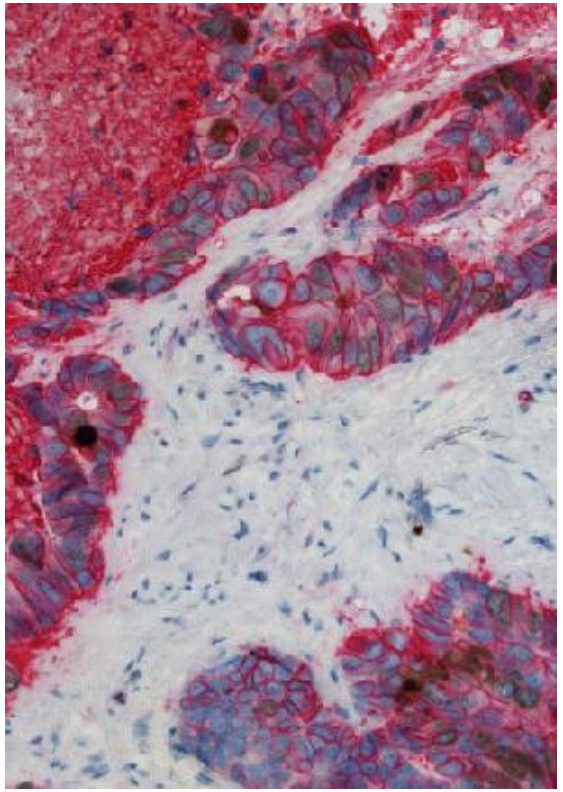
MIV-818 shows activity in hypoxic regions of liver tumours

- Equal frequency of pH2AX positive nuclei observed in regions of high membrane Glucose transporter 1 (Glut1) staining
- Indicates that MIV-818 reaches hypoxic areas and induces DNA-damage (common limitation for chemotherapy)

Glut1 membrane expression (hypoxia)



Data from Patient 2



Data from Patient 4

MEDIVIR

Phase Ia – summary preliminary data

- MIV-818 has been well tolerated, but the findings suggests an impact from dosing and that we are close to a maximum tolerated dose
- Clear signs of effect, measured as DNA damage, observed in liver biopsies from tumor tissue in MIV-818 treated patients. Normal liver tissue does not appear to have been affected
- This tumor selective effect was observed at low levels of MIV-818 in plasma and is an early indication that MIV-818 has the intended liver-directed effect

Next steps

- The results from the first six patients are very positive
- Medivir has decided to initiate the phase Ib part of the MIV-818 study as soon as the independent safety committee has given its recommendation on an appropriate starting dose.
- A few more patients will be recruited in phase Ia to ensure that the dose-selection is optimal

Q and A

MEDIVIR