2023 ESMO TAT

Targeted Anticancer Therapies

PRELIMINARY RESULTS FROM A PHASE IA TRIAL OF SELECTIVE FGFR1-3 INHIBITOR CPL304110 IN PATIENTS WITH FGFR-DEREGULATED ADVANCED SOLID MALIGNANCIES

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ClinicalTrials.gov ID: NCT04149691

CELON PHARMA

NCBR National Centre for Research and Development

STRATEGMED

Instytut Gruźlicy i Chorób Płuc

WIM

Medical University of Gdańsk

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Maria Skłodowska-Curie National Research Institute of Oncology

WMC

BRG BioResearch Group

Europejskie Centrum Zdrowia Otwock

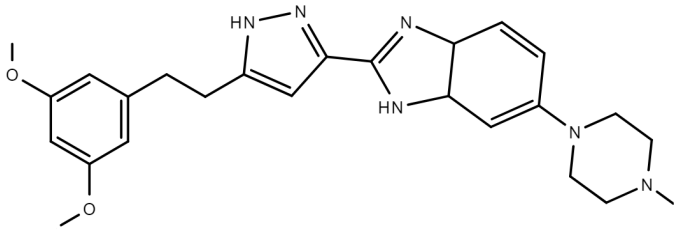
CONFLICT OF INTERESTS

Honoraria:	ROCHE, MSD, BMS, AMGEN, JANSSEN, ASTRA, MICROGENICS, INCYTE, SANOFI, TAKEDA, SIROPA, RHIZEN, MENARINI, RYVU, CHECKPOINT THERAPEUTICS, PFIZER, BOEHRINGER INGELHEIM
Research funds:	NCBR, ABM, ROCHE
Travel grants:	CELON, BMS, ROCHE
Advisory role:	ROCHE, MSD, BOEHRINGER INGELHEIM

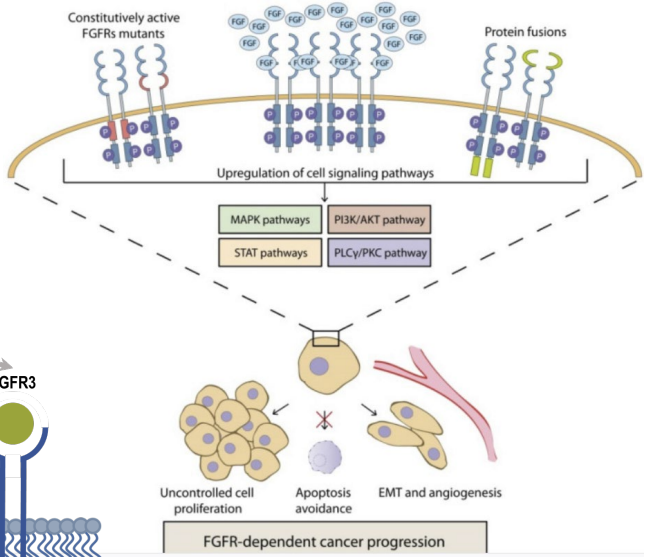
FIBROBLAST GROWTH FACTOR RECEPTORS (FGFRs)

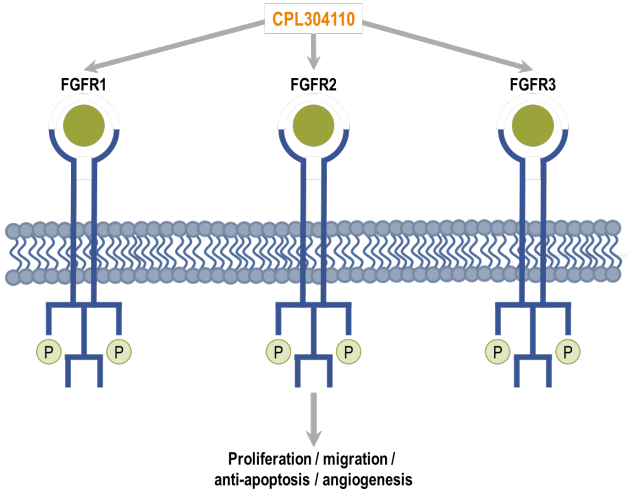
Molecular targets in oncology

- **CPL304110** – new tyrosine kinase inhibitor of FGFR 1–3
- benzodiazole derivative in the formulation of hard gelatin capsule



Szymczyk J, Cancers 2021
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8616288/





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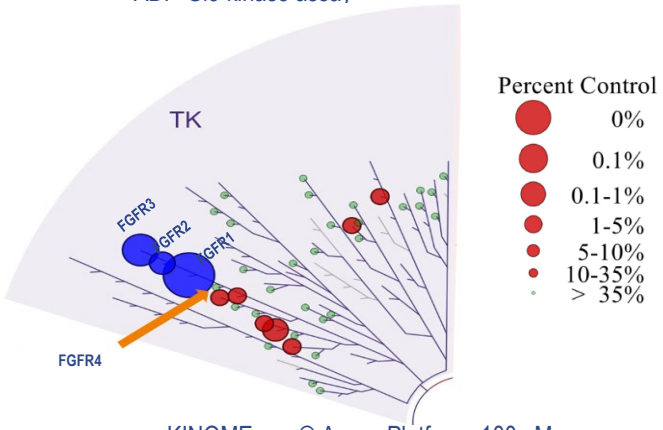
CPL304110 – POTENT AND SELECTIVE FGFR1-3 INHIBITOR

High *in vitro* activity against FGFR1-3 and selectivity over FGFR4

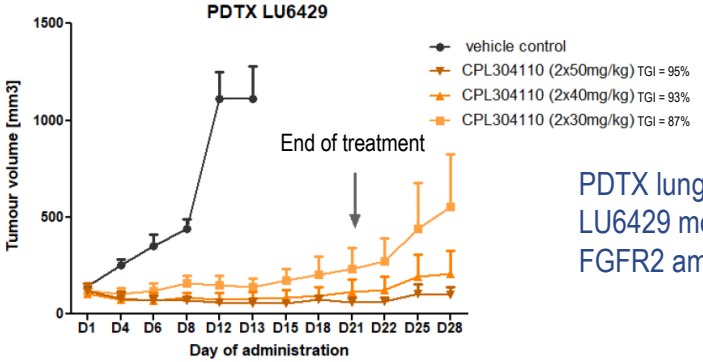
IC_{50} [nM]			
FGFR1	FGFR2	FGFR3	FGFR4
0.75	0.5	3.5	87.9

ADP-Glo kinase assay

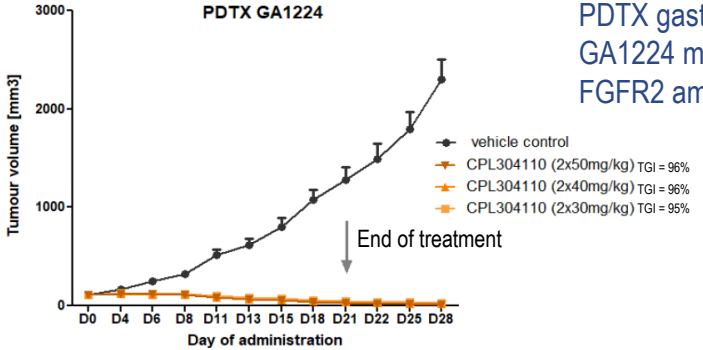


KINOMEscan® Assay Platform, 100 nM
Tyrosine Kinases

High *in vivo* activity in patient derived xenograft models (PDTXs)



PDTX lung cancer model:
LU6429 model with
FGFR2 amplification



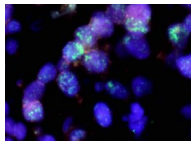
PDTX gastric cancer model:
GA1224 model with
FGFR2 amplification

STUDY DESIGN

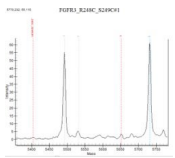
Key objectives:

- determine safety and tolerability of CPL304110
- establish recommended phase II dose
- evaluate pharmacokinetics

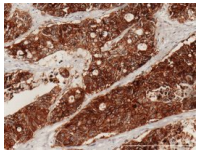
Amplification – FISH



Mutation – MALDI-TOF MS

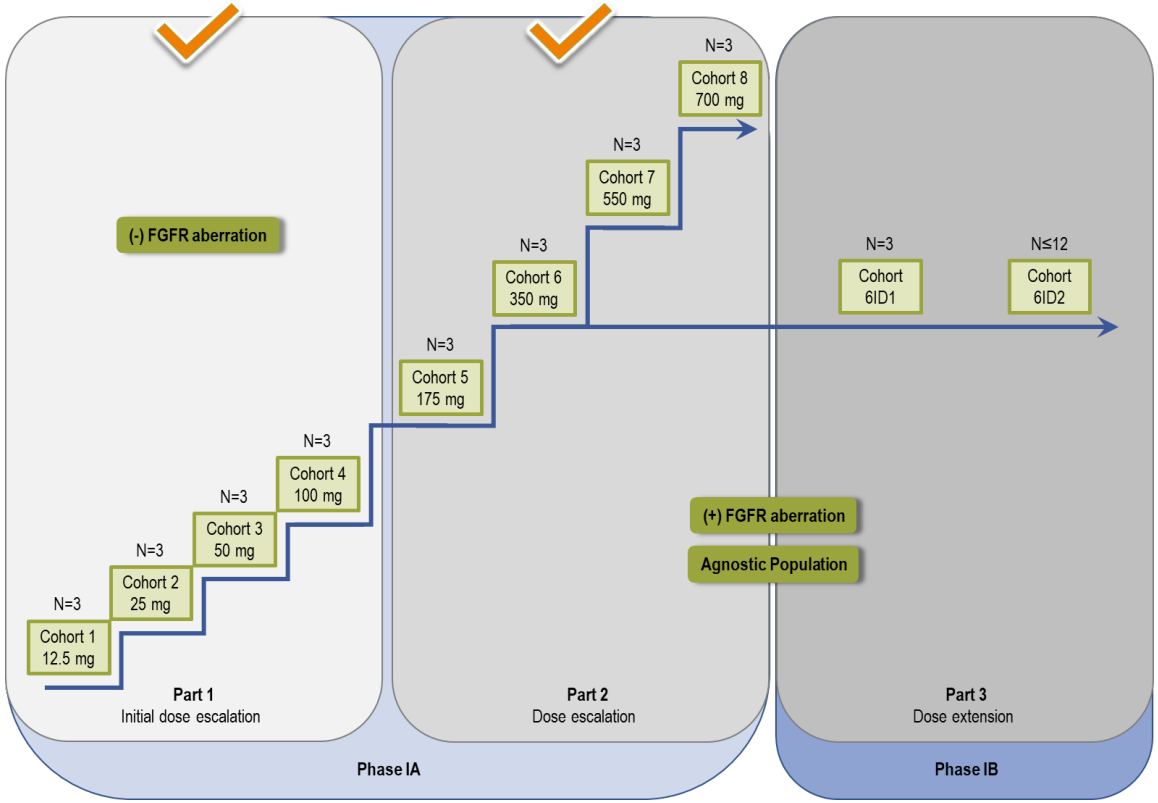


Expression – IHC



Diagnostic test approved by regulators

FOUNDATION MEDICINE®



INCLUSION CRITERIA

Specific for part 1	Specific for part 2

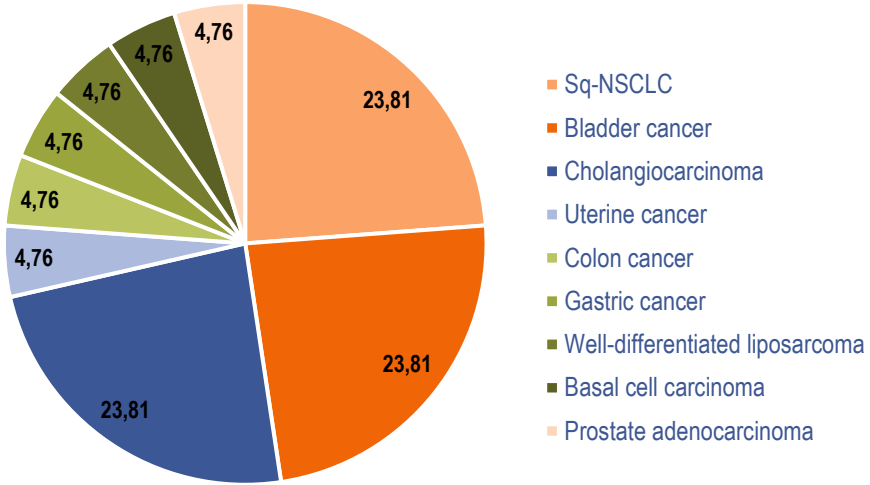
• Advanced histologically confirmed:
  • Gastric cancer
  • Bladder cancer
  • Squamous lung cancer or NSCLC with squamous immunophenotype (NSCLC favour squamous cell carcinoma)
  • Cholangiocarcinoma
  • Sarcoma
  • Endometrial cancer
	• **Exploratory Cohort with confirmed FGFR1-3 molecular alteration**
	
	FGFR aberration status confirmed with diagnostic tests approved by regulators AND/OR performed in diagnostic laboratories AND/OR developed by the Sponsor

General eligibility criteria	
• Age of ≥25 y.; • Refractory to prior therapies; • Measurable disease according to RECIST version 1.1; • ANC ≥ 1.5 × 109/L; • Haemoglobin ≥ 9.0 g/dL; • Platelet count ≥ 100 × 109/L;	• ALT and AST ≤ 2.0 ULN, in liver mets ≤ 5 ULN, ALP ≤ 2.5 ULN; • Total bilirubin ≤ 1.5 ULN; • Serum creatinine ≤ 1.5 ULN; • PTH 10 - 60 pg/mL, TSH within normal range; • Albumin ≥ 2.5 g/dL; • Phosphate levels within normal range

STUDY POPULATION

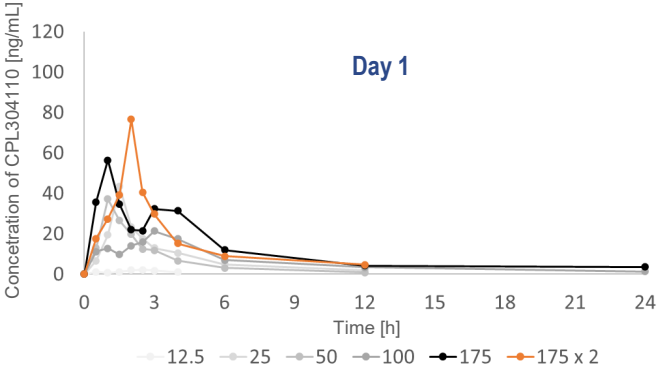
Patients at baseline		
Characteristics		**Number (n=21)**
Sex (%)	Male	14 (66.67)
	Female	7 (33.33)
Median age		63 (43-74)
Median of previous anticancer regimens		2 (1-4)

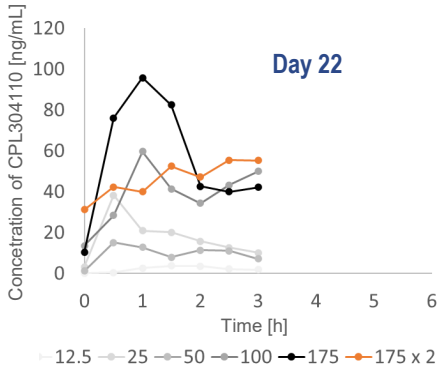
Type of cancer (%) in the studied population (N=21)



PHARMACOKINETICS PROFILE OF CPL304110

Mean concentration of CPL304110 in human plasma after administration of doses 12.5-175 mg once daily and 175 mg twice daily





Cohort	Dose [mg]	N	C_{max} [ng/mL]	t_{max} [a] [h]	$t_{1/2}$ [h]	AUC_{0-t} [ng/mL*h]
1	12.5	3	3.3	1.5	n/a	7.0
2	25	3	31.4	1.0	n/a	76.8
3	50	4[b]	23.8	1.5	n/a	50.4 [d]
4	100	5[c]	50.9	2.5	8.8 [d]	150.6 [d]
5	175	3	92.0	1.5	11.5 [d]	262.4
6	2 x 175	3[e]	100.1	1.5	6.2 [d]	317.8

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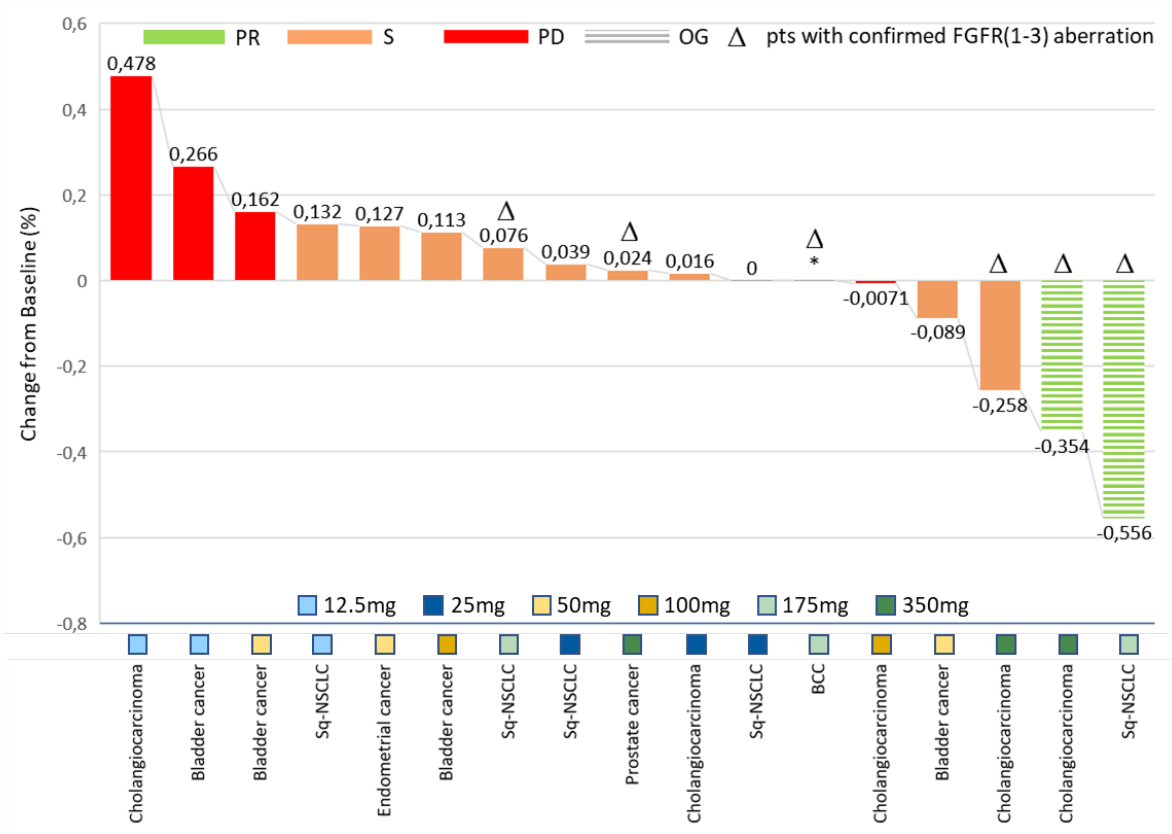
SAFETY OF CPL304110

Adverse event	Any Grade	Grade 3	Grade ≥ 4
Ocular toxicity*	5 (23.8%)	-	-
Anemia	4 (19%)	-	-
Dry eye	3 (14.3%)	-	-
Dry mouth	3 (14.3%)	-	-
ALT increased	2 (9.5%)	-	-
Xerostomia	2 (9.5%)	-	-
Hiperfosfatemia	2 (9.5%)	-	-
AST increased	2 (9.5%)	-	-
Onychodystrophy	2 (9.5%)	-	-
Constipation	2 (9.5%)	-	-
Fatigue	2 (9.5%)	-	-
Cough	1 (4.8%)	-	-
Increased creatinine	1 (4.8%)	-	-
Stomach ache	1 (4.8%)	-	-
Blood 1,25-dihydroxy vitamin D decreased	1 (4.8%)	-	-
Lack of appetite	1 (4.8%)	-	-
Bradycardia	1 (4.8%)	-	-
Oral cavity fungal infection	1 (4.8%)	1 (4.8%)	-
Dry mouth mucosa	1 (4.8%)	-	-

Adverse event	Any Grade	Grade 3	Grade ≥ 4
Discoloration of fingernails and toenails	1 (4.8%)	-	-
Ventricular arrhythmia or asymptomatic ventricular arrhythmia	1 (4.8%)	-	-
Inflammation of the skin of the corners of the mouth	1 (4.8%)	-	-
Vomiting	1 (4,8%)	-	-
Nausea	1 (4.8%)	-	-
Chest pain	1 (4.8%)	-	-
Damage to the skin of the pads of the fingers	1 (4.8%)	-	-
Haemoptysis	1 (4.8%)	-	-
PTH low	1 (4.8%)	-	-
Hand-foot syndrome	1 (4.8%)	-	-
Taste changed	1 (4.8%)	-	-
Atrial fibrillation	1 (4.8%)	-	-
Hypercalcaemia	1 (4.8%)	-	-
Weakness	1 (4.8%)	-	-
GGTP increased	1 (4.8%)	-	-
ALP increased	1 (4.8%)	1 (4.8%)	-

* decreased vision, fluid under the retina, subretinal deposits

PRELIMINARY EFFICACY OF CPL304110



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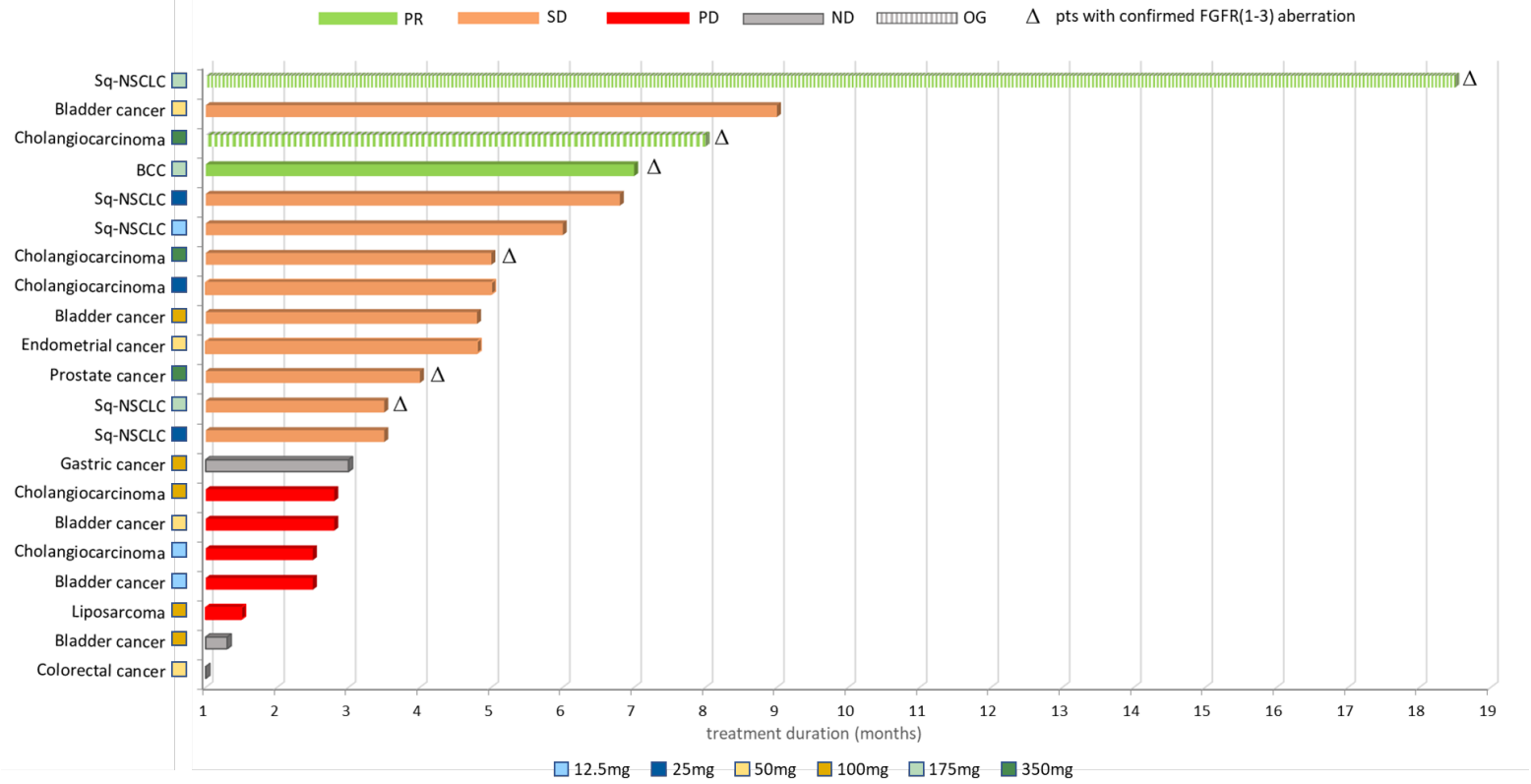

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CONCLUSIONS

- CPL304110 administration is associated with acceptable toxicity.
- Preliminary results suggest low potential for CPL304110 accumulation and linear pharmacokinetics
- Encouraging response rates were observed in heavily pretreated patients, especially in the agnostic group of patients with confirmed FGFR(1-3) aberration in advanced solid malignancies, with the first observed response at dose 175mg QD.
- The clinical trials assessment in extension part is ongoing

FUNDING

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NCBR National Centre for Research and Development

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Targeted Anticancer Therapies

Thank you for your attention

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