Efficacy and safety of SABR with TKI and IO therapy in patients with mRCC

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Clinical trial information: ChiCTR2200059204

Background

- In Metastatic RCC TKI in combination with IO has become a standard therapy
- Some pts may present with oligo-metastasis or with metastatic site related symptoms
- SABR (Stereotactic Ablative Body Radiotherapy) has been proved to be highly effective for RCC with potential immune enhancing ability
- Purpose of present study is to investigate efficacy and safety of SABR with TKI and IO therapy in pts with mRCC

Methodology

Study Design	• Ambispective cohort study
Inclusion Criteria	• mRCC pts receiving SABR with TKI and IO at the same time
Adverse events	• Evaluated according to CTCAE 5.0
Primary End Point	• PFS
Secondary end points	• OS, ORR, DCR and TTTC (Time to treatment change)
Additional Sub study	• Some of the pts gene characteristics were analysed to investigate the relationship between gene alterations and prognosis

Results

- Study Period: (till August 2024)
  - Retrospectively pts from Mar 2020 - Mar 2024
  - Prospectively pts from Mar 2024 - May2024
- N= 79 pts
- 72.2% were with ccRCC
- 68.4% were with oligo-metastases (#5 meta sites)
- 83.5% were combined with SABR before 1st-line systemic therapy failure

Results……

International Metastatic RCC Database Consortium (IMDC):

- Intermediate or poor prognosis group

TKI and IO combination was used in all patients

All pts with oligo-metastases received SABR for all tumor sites and others were for cytoreductive purpose

Results: Follow Up

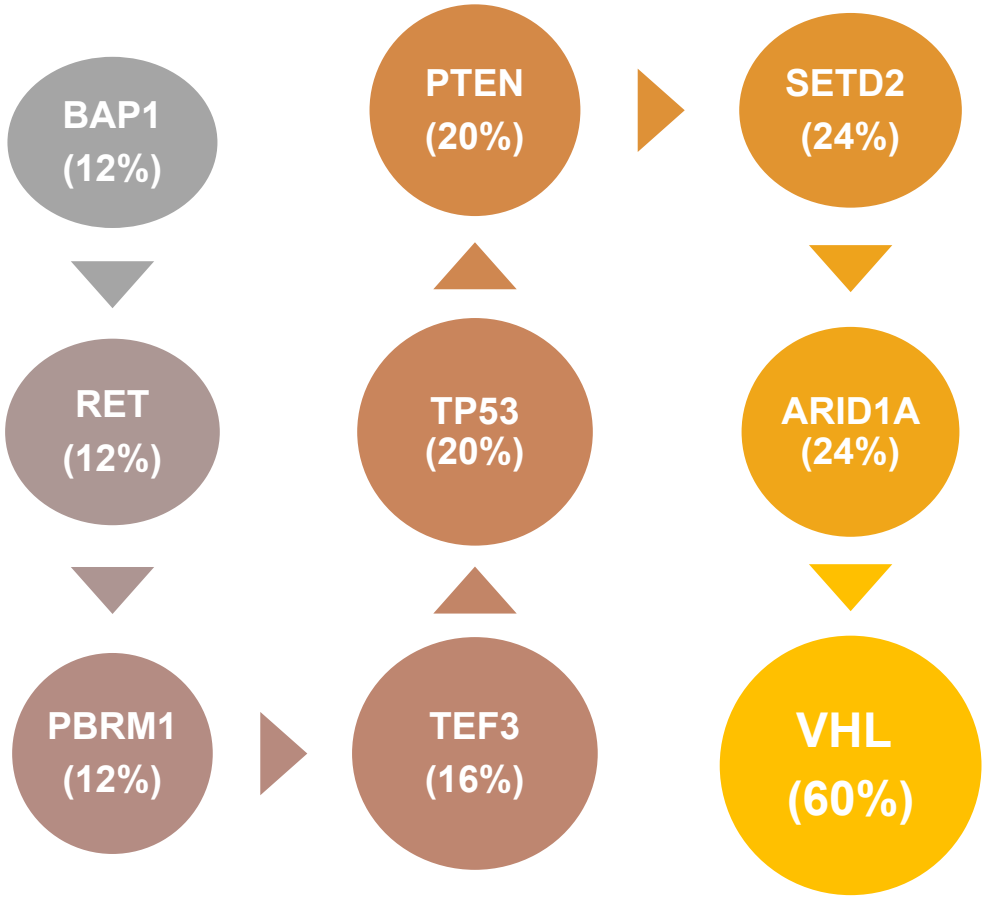
Median follow-up	• 20.3 months
Median Progression free survival	• 28.6 months
Time to treatment Change	• 31.8 months
Overall Response Rate	• 68.4%
Disease Control Rate	• 89.9%
DCR of Radiation lesions	• 96.2%
Median Overall Survival	• 44.8 months

For pts received SABR before or after 1st-line systemic therapy failure, PFS were 30.6 months vs.9.6 months, respectively (p=0.004)

Results: NGS Analysis

N= 25 pts tumor samples

- **Favourable trend for PFS** in pts with tumors purely driven by VHL loss
- Mutations in mTOR pathway genes, PTEN and HRR-related genes appeared to lead to **poorer PFS**
- Due to limited sample size, statistical significance was not reached



Adverse Events

- Grade 3 or above AE was 50.2%
- There was no treatment-related death

SABR trials with TKI / IO in mRCC

Trial	Study Design	Population	Intervention	Systemic Therapy	Primary Endpoint	Key Findings / Notes
SABR for Oligoprogression in mRCC on TKI (2021)	Phase II, Prospective, Multicenter	mRCC with oligoprogression (1–5 progressing lesions) on stable TKI	SABR to oligoprogressive sites	Ongoing TKI (e.g., sunitinib, pazopanib)	PFS after SABR	• SABR delayed systemic switch in >50% of patients • Safe and effective in prolonging TKI efficacy • Median PFS 9.3 months
Lalani et al. CYTOSHRINK (ASCO 2023)	Phase II	mRCC with intact primary	SBRT (Primary) 30-40Gy/5fr between 1 and 2 cycles **(Cytoreductive)**	Nivolumab + Ipilimumab	Feasibility, local control, immune modulation	Ongoing
NRG-GU012 (SAMURAI) (ASCO 2023)	Randomized Phase II	mRCC with unresected metastases	SABR to 1–5 lesions **(Cytoreductive)**	IO (Ipi/Nivo, Nivo+Cabo)	PFS at 1 year	**Ongoing** • Aims to test SABR synergy with IO in upfront mRCC
RAPPORT Trial (2022)	Phase I/II	Oligometastatic RCC (≤3 sites)	SABR to all sites	Short-course pembrolizumab (4 cycles)	Safety and efficacy (PFS, ORR)	• SABR + pembro safe, with 39% ORR and 82% local control at 1 year • Limited pembro exposure
SABR with TKI and IO in mRCC (ASCO 2025)	Phase II	mRCC with ≤5 mets	SABR to all sites	TKI (e.g., axitinib) + IO (pembrolizumab)	ORR, PFS, toxicity	• Early data show promising PFS (~10–12 months) • Manageable toxicity Synergy of all three modalities

Conclusions

- Targeted therapy + immunotherapy + stereotactic radiotherapy has achieved satisfactory survival results for mRCC

- Early intervention by SABR may lead to a better PFS

Thank You