Cytoreduktivní nefrektomie v éře imunoterapie a tyrozinkinázových inhibitorů

Poprach A, Lakomý R

MOU a LF MU, Brno

Definice cytoreduktivní nefrektomie:

- „Cytoreductive nephrectomy (CN) is defined as the surgical removal of the primary RCC lesion **before** initiation of systemic therapy.“

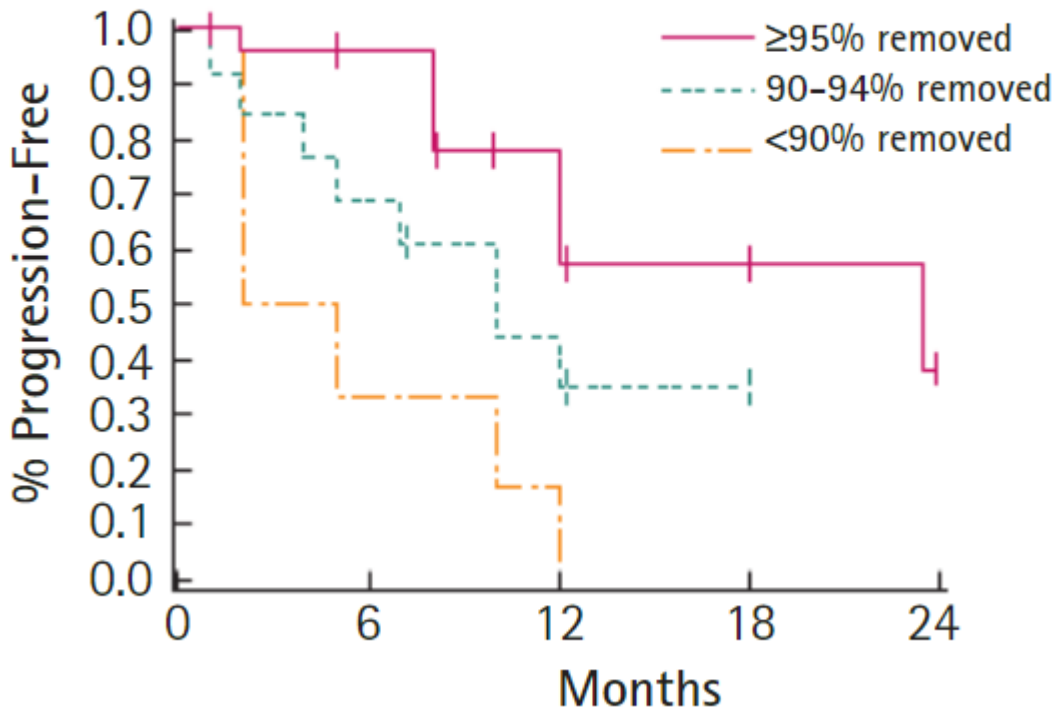
- „Cytoreductive nephrectomy (CN), defined **as removal of the kidney and primary tumour in the face of metastatic disease**, was historically described in association with occasional regression of metastatic deposits.“

- Jasná definice, zdá se není…ale bylo zvykem, že CN se provádí **před** systémovou léčbou.

Larcher A, et al., Eur Urol Oncol 2019

Problematická je však analýza dat, obvzláště retrospektivně (bias)

- Cytoreduktivní nefre ebo jiné strategie v rámci mRCC - watch na *FIG. 1. PFS by FPTV.* vě“???
- V řadě studií se kons arciální“
- Nerozlišuje se mezi
- Není mnoho studií (ento výkon v určitém intervalu do
- Prospektivní studie (čekáme
- CYTOREDUKTIVNÍ N !!![1]



[1]Barbastefano et al, BJUI 2010;106:1266

Prognostické modely MSKCC vs. IMDC

1999, 3 skupiny (0…1+2…3 a více)

1. KPS < 80%
2. Hem < pod normu
3. Korig.vápník v séru> nad normu
4. LDH> 1,5 x horní hranice normy
5. Přítomnost či nepřítomnost nefrektomie

The model reported in this article categorized patients into three distinct groups with median survival times of 20, 10, and 4 months. The criteria was based on history of nephrectomy, performance status obtained at physical examination, and assessment of hemoglobin, lactate dehydrogenase, calcium, and albumin (to assess corrected calcium) performed as routine blood tests. Nephrectomy was not performed for the purpose of cytoreduction before the start of systemic therapy. The patient population was selected by fulfilling individual protocol eligibility criteria. For example, patients with brain metastases were excluded. However, the experi-

2009

1. KPS < 80%
2. Hem < norma
3. Korig.vápník v séru> nad normu
4. Doba od diagnózy do léčby (< 1 rok)
5. Abs.počet neutrofilů > norma
6. Trombocyty > norma

Motzer et al., JCO 1999
Heng et al, JCO 2009

Nefrektomie v rámci mRCC v éře TKI (CARMENA)

- IMDC kritéria; 1 nebo 2 rizikové faktory

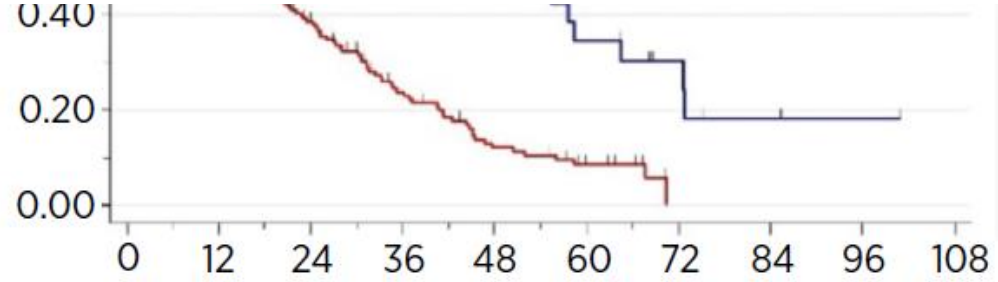
CN je tedy vhodná u pt s jedním rizikovým faktorem, především jen s plicními mts a u pt s ORR typu PR a CR na TKI.
CAVE: a ještě v dobré prognostické skupině, oligomts onemocněním, zřejmě i symptom. primárním nádorem.

Medián celkové

Median OS, months (95% CI)
IMDC 1 risk factor
IMDC 2 risk factors

edián OS (měsíce)
44 (23,3-64,6)
31,5 (14,7-64,4)
1,24 (0,62-2,47)

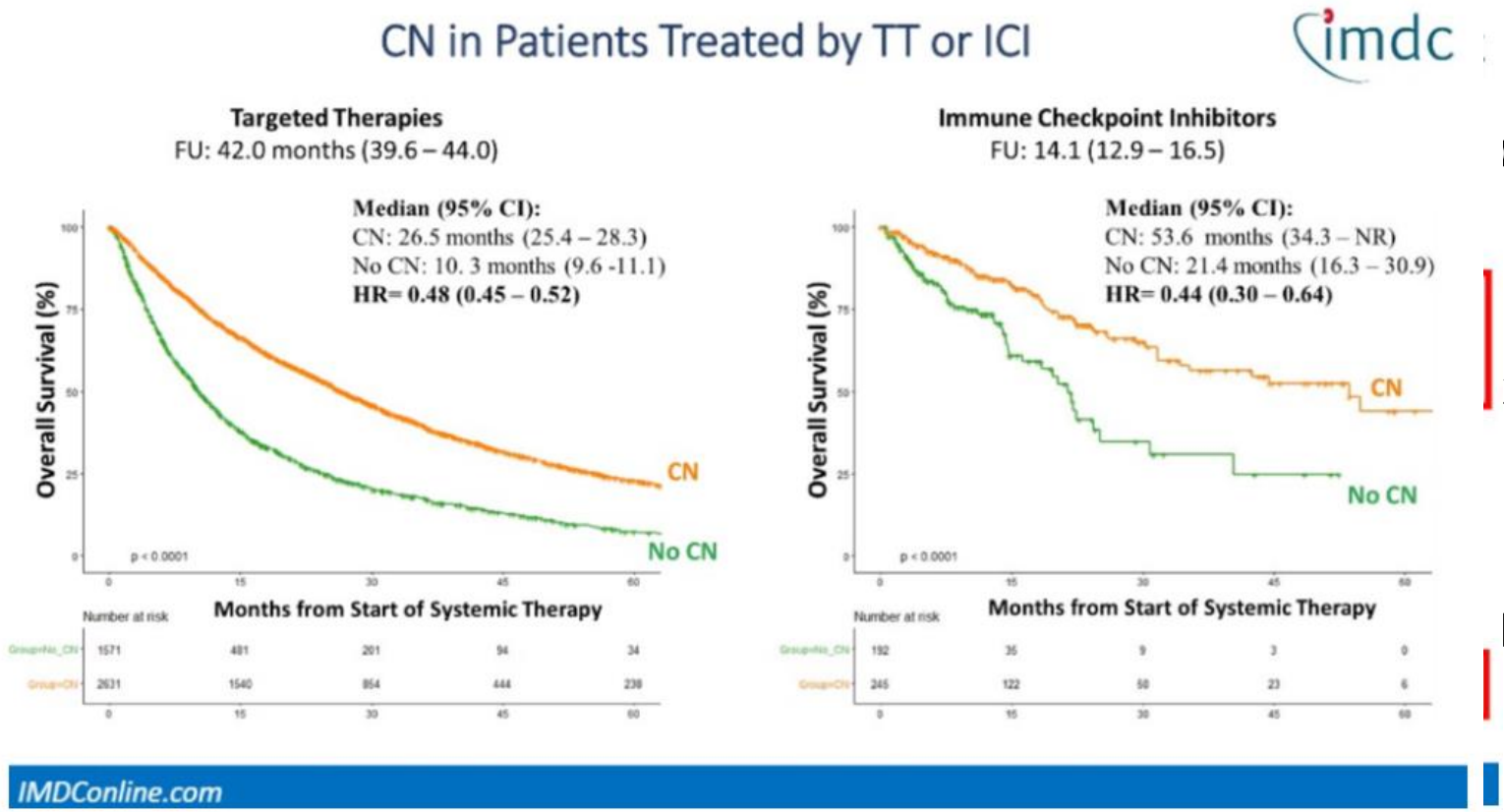
- Navíc ...cení, bolest, ci dobra iecer... pak **48,5 vs. 15,7 měsíce**



Mejean A, et al., J Clin Oncol 2019, abs

Nefrektomie v rámci mRCC, imunoterapie???

- Vyčka
  -)C rizikové faktory),
  - xi a +/-
  - primární léze a poté
- Ale n

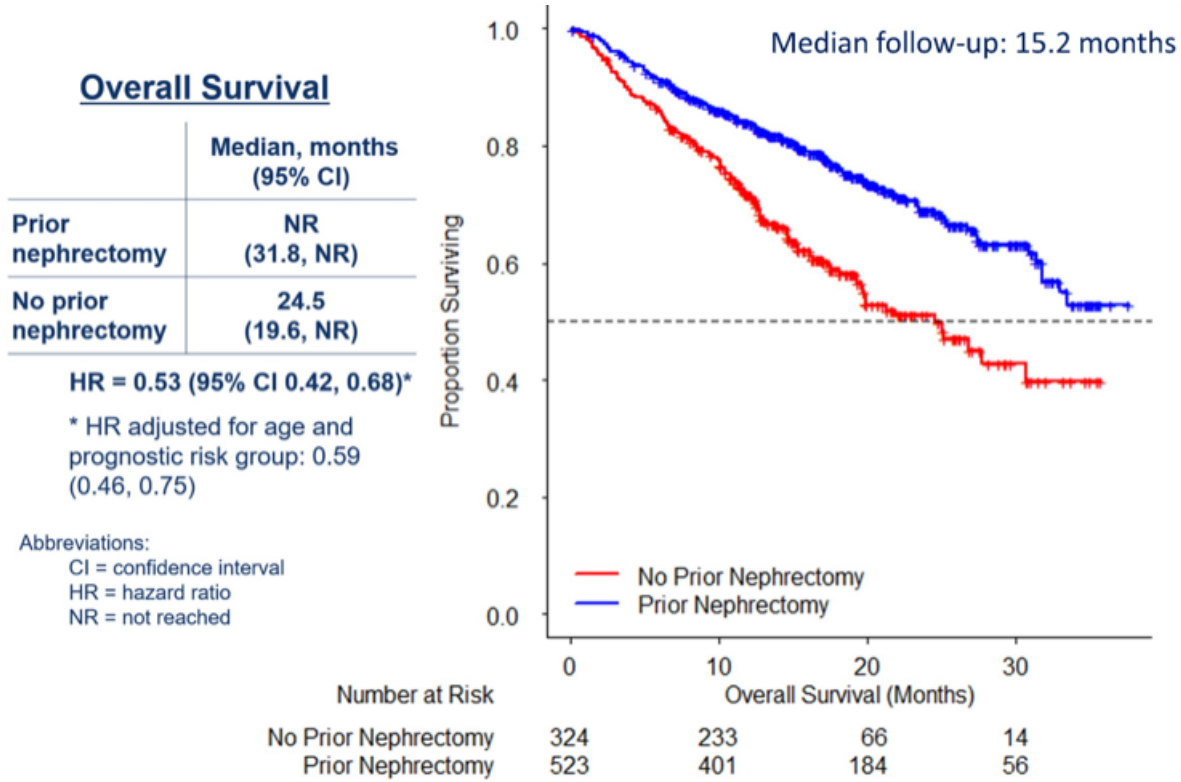


Bakouny et al, abst 608 ASCO 2020

Nefrektomie v rámci mRCC, imunoterapie???

- A nověji i z ASCO 2021, v retrospektivní práci autoři důsledně trvali na cytoreduktivní nefrektomii (ne v minulosti prodělané CN)!

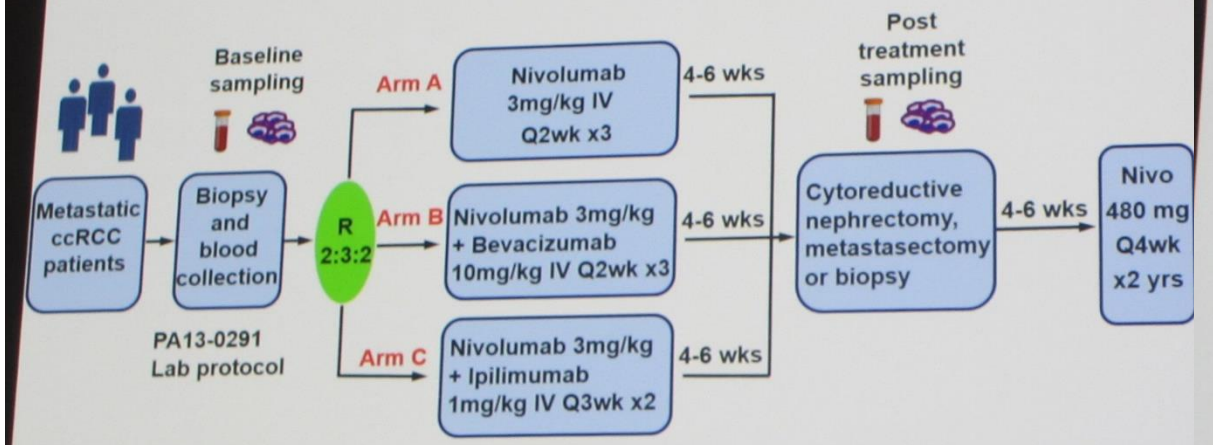
Pts with stage IV RCC at initial dx (N = 849)	Prior Nephrectomy (N = 523)	No Prior Nephrectomy (N = 326)	HR (95% CI)
Age, mean (SD)	59.8 (9.3)	62.3 (10.3)	
Months from diagnosis to randomization, median (IQR)	3.4 (1.9, 8.0)	1.5 (1.0, 2.5)	
Death events N (%)	139/523 (27%)	134/326 (41%)	
Favorable risk	9/44 (20%)	10/37 (27%)	0.69 (0.28, 1.72)
Intermediate risk	93/397 (23%)	80/200 (40%)	0.47 (0.35, 0.64)
Poor risk	37/82 (45%)	44/87 (51%)	0.84 (0.54, 1.30)
Median OS (unadjusted HR)	NR (31.8, NR)	24.5 (19.6, NR)	0.53 (0.42, 0.68)
Median OS (HR adjusted for age and prognostic risk group)	NR (31.8, NR)	25.2 (19.8, NR)	0.59 (0.46, 0.75)



Fallah et al. ASCO 2021

RCC nefrektomie u IT

Trial Schema (NCT02210117; CA209-173)

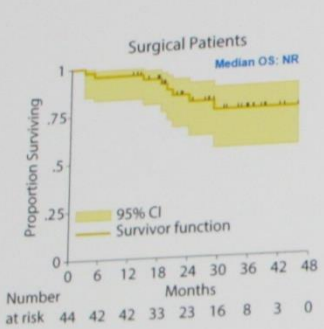


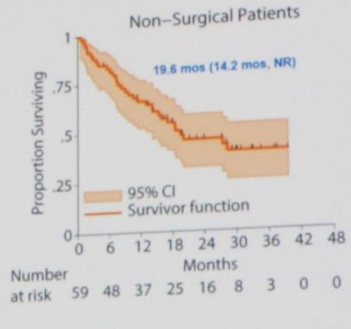
- Total accrual: 104 patients (Median follow up: 29 mos)
- Primary endpoint: Safety
- Secondary endpoints: Biomarker; BOR, OS, PFS
- This trial was NOT designed to compare clinical outcomes between arms

Clinical Responses in Patients with or without Surgery

		Nivo N=29	Nivo+Bev N=45	Nivo+Ipi N=30
Response Measure	Surgery Status	N (%)	N (%)	N (%)
BOR[1]	All Patients	17/29 (59%)	20/45 (44%)	13/30 (43%)
	Surgical Patients[2]	12/14 (86%)	14/16 (82%)	9/13 (69%)
	Non-Surgical Patients	5/15 (33%)	6/29 (21%)	4/17 (24%)
Disease Control (CR + PR +SD)	All Patients	20/29 (69%)	27/45 (60%)	15/30 (50%)
	Surgical Patients	13/14 (93%)	15/16 (94%)	10/13 (77%)
	Non-Surgical Patients	7/15 (47%)	12/29 (43%)	5/17 (29%)

Overall Survival for Surgical and Non-Surgical Patients



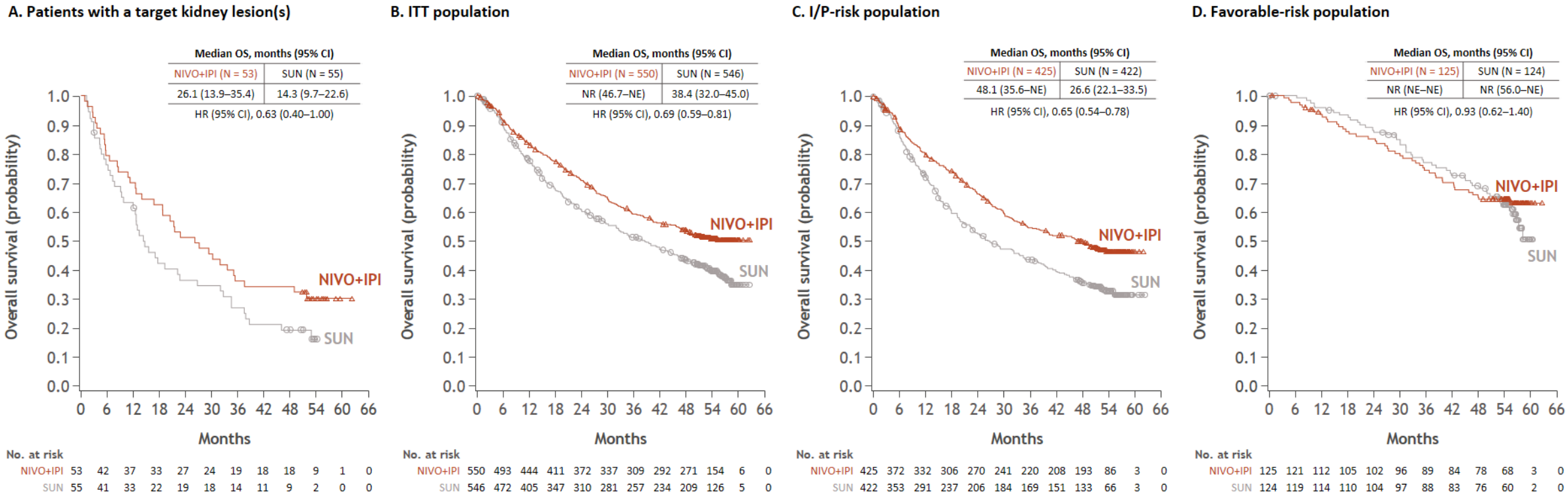


Surgery Status	2-Year Estimate	Standard Error
Yes	84%	6%

Surgery Status	2-Year Estimate	Standard Error
No	46%	7%

Gao et al. 2019, ASCO

IO a její účinnost na primární renální léze?, studie CHECKMATE 214



Albiges L et al. ESMO 2020

IO a její účinnost dle provedení nefrektomie, studie CHECKMATE 9ER

Outcome	With prior nephrectomy		Without prior nephrectomy	
	NIVO + CABO (n = 222)	SUN (n = 233)	NIVO + CABO (n = 101)	SUN (n = 95)
Confirmed ORR (95% CI), %	60.8 (54.1-67.3)	30.5 (24.6-36.8)	41.6 (31.9-51.8)	23.2 (15.1-32.9)
Best overall response, n (%)				
Complete response	25 (11.3)	14 (6.0)	5 (5.0)	0
Partial response	110 (49.5)	57 (24.5)	37 (36.6)	22 (23.2)
Stable disease	67 (30.2)	93 (39.9)	41 (40.6)	43 (45.3)
Progressive disease	13 (5.9)	31 (13.3)	7 (6.9)	14 (14.7)
Unable to determine	7 (3.2)	38 (16.3)	11 (10.9)	15 (15.8)
Not reported	0	0	0	1 (1.1)
Median (Q1-Q3) time to response, months	2.8 (2.8-3.3)	4.1 (2.8-7.1)	2.8 (2.8-5.4)	5.5 (4.0-8.3)

Porta C et al, ESMO 2020

Metastezektomie: standard v léčbě mRCC

- Musí být správně indikovaná:
  - Oligomts onemocnění
  - Progredující onemocnění „v jednom místě“ při systémové léčbě
  - Přetrvávající mts při jinak dosažené CR
  - Operace komplikující mts (obratle, krvácející mts…)…viz CARMENA (primum) a Méjean „střelení do nohy „(samocitace ASCO 2019), s výhodou při systémové léčbě
- Pak je ale plně i**ndikováno odstranění prima**, které zřídkakdy **plně** odpoví na systémovou léčbu
- **Otázka není zda…ale u koho a kdy provést tuto operaci?**

Stereotaktické radioterapie, mRCC

Lancet Oncol. 2021 Dec;22(12):1732-1739. doi: 10.1016/S1470-2045(21)00528-3. Epub 2021 Oct 28.

Definitive radiotherapy in lieu of systemic therapy for oligometastatic renal cell carcinoma: a single-arm, single-centre, feasibility, phase 2 trial

Chad Tang [1], Pavlos Msaouel [2], Kieko Hara [3], Haesun Choi [4], Venus Le [5], Amishi Y Shah [6], Jennifer Wang [6], Eric Jonasch [6], Seungtaek Choi [5], Quynh-Nhu Nguyen [5], Prajnan Das [5], Surendra Prajapati [7], Zhiqian Yu [7], Khaja Khan [3], Steven Powell [3], Ravi Murthy [8], Kanishka Sircar [9], Nizar M Tannir [6]

Affiliations + expand

PMID: 34717797 DOI: 10.1016/S1470-2045(21)00528-3

Abstract

Background: The role of radiotherapy in metastatic renal cell carcinoma is controversial. We prospectively tested the feasibility and efficacy of radiotherapy to defer systemic therapy for patients with oligometastatic renal cell carcinoma.

Methods: This single-arm, phase 2, feasibility trial was done at one centre in the USA (The MD Anderson Cancer Center, Houston, TX, USA). Patients (aged ≥18 years) with five or fewer metastatic lesions, an Eastern Cooperative Oncology Group status of 0-2, and no more than one previous systemic therapy (if this therapy was stopped at least 1 month before enrolment) without limitations on renal cell carcinoma histology were eligible for inclusion. Patients were treated with stereotactic body radiotherapy (defined as ≤5 fractions with ≥7 Gy per fraction) to all lesions and maintained off systemic therapy. When lesion location precluded safe stereotactic body radiotherapy, patients were treated with hypofractionated intensity-modulated radiotherapy regimes consisting of 60-70 Gy in ten fractions or 52·5-67·5 Gy in 15 fractions. Additional rounds of radiotherapy were allowed to treat

gomts či „v jednom místě“

cell carcinoma: radiotherapy as a new

ell carcinoma
of 9·5%.[1] In
rgery remains
radiotherapy
patients with
past 20 years,
owed targeted
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of surrounding
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prospective analysis of 30 patients with 82 secondary renal cancer lesions, local control rate with SBRT was nearly 98%, with a median overall survival of 32 months.[7] The number and size of metastatic lesions outside the field of radiation were shown to reduce due to the abscopal effect via an immune response and the secretion of antitumour and antiangiogenic factors. Thus, with the delivery of high doses per fraction, SBRT was a minimally invasive and effective treatment for metastatic renal cell carcinoma.[8] The integration of SBRT into the holistic management of patients with oligometastatic renal cell carcinoma might have a positive effect on the systemic control of the disease by postponing the introduction of systemic treatments.

Magne et al, Lancet; Tang C, Lancet 2021

Závěr, pro případy ponechaného tumoru in situ

- **Bez CN to asi k CR nepovede ani v době IO**….zde si vedou trochu lépe TKI…**resp. kombinace TKI a IO!!!**

- Není třeba chodit pro informace daleko- viz edice Solen 01 / 2022- článek doc. Vošmik- STX radioterapie prima a mts, **abskopální efekt…není mlha na vzdáleném obzoru! (je to spíše nevyzkoušené a proto v ČR zatím málo používané)**

  - **Není radioterapie (konvenční) jako radioterapie (STX)**

- **Není zřejmě nutný přesný nůž operatéra, jen ta KOMBINACE s systémovou léčbou!!!!, antigeny!!!**

- MULTIOBOROBÉ KOMISE…buďme stateční, zkusme nejen všechny linie, pokud je to možné, ale i terapeutické postupy!!!...cíl je CR!!! (resp. dlouhodobá kontrola onemocnění)

- DĚKUJI ZA POZORNOST

Tati, na klouzačce je saranče!!!

Kobylka zelená
(Tettigonia viridissima)