VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

1. LÉKAŘSKÁ FAKULTA Univerzita Karlova

# Role cytoredukční nefrektomie v éře imunoterapie

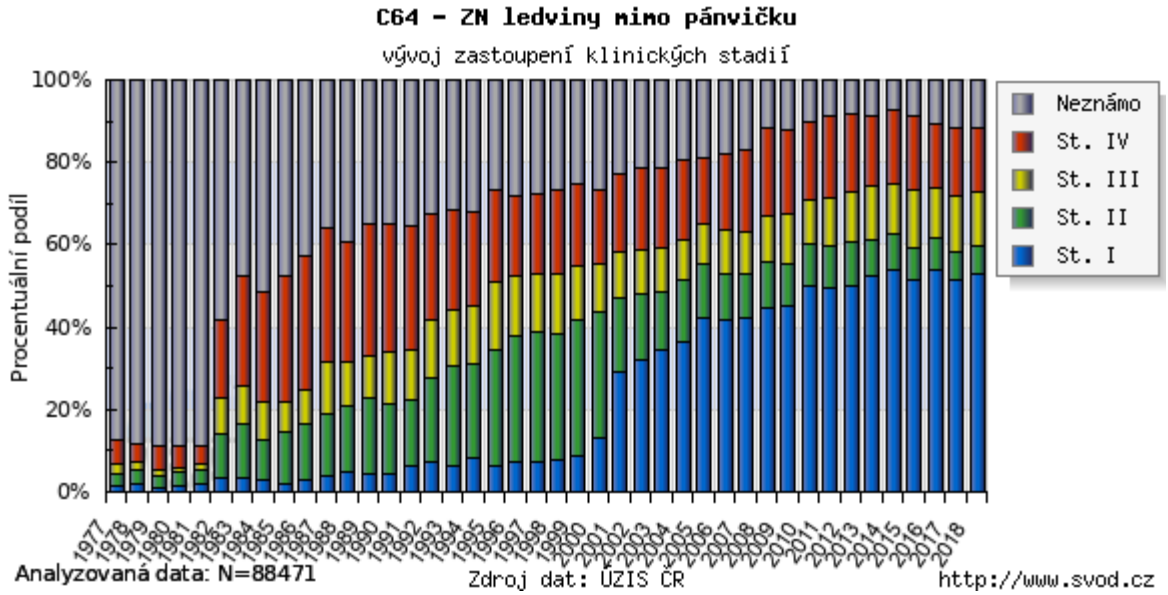
Vojtěch Fiala

Urologická klinika VFN a 1.LF UK v Praze

PragueOnco 2022

# Renální karcinom - metastatický

- Ročně diagnostikováno kolem 3000 pac. s karcinomem ledviny
- 15,5% za rok 2018 (≈16%)



# Změna přístupu

- Studie CARMENA (Méjean et al., 2018) – „samotný Sunitinib není inferiorní v porovnání s nefrektomií a následně podávanému Sunitinibu“
  - Update 2021

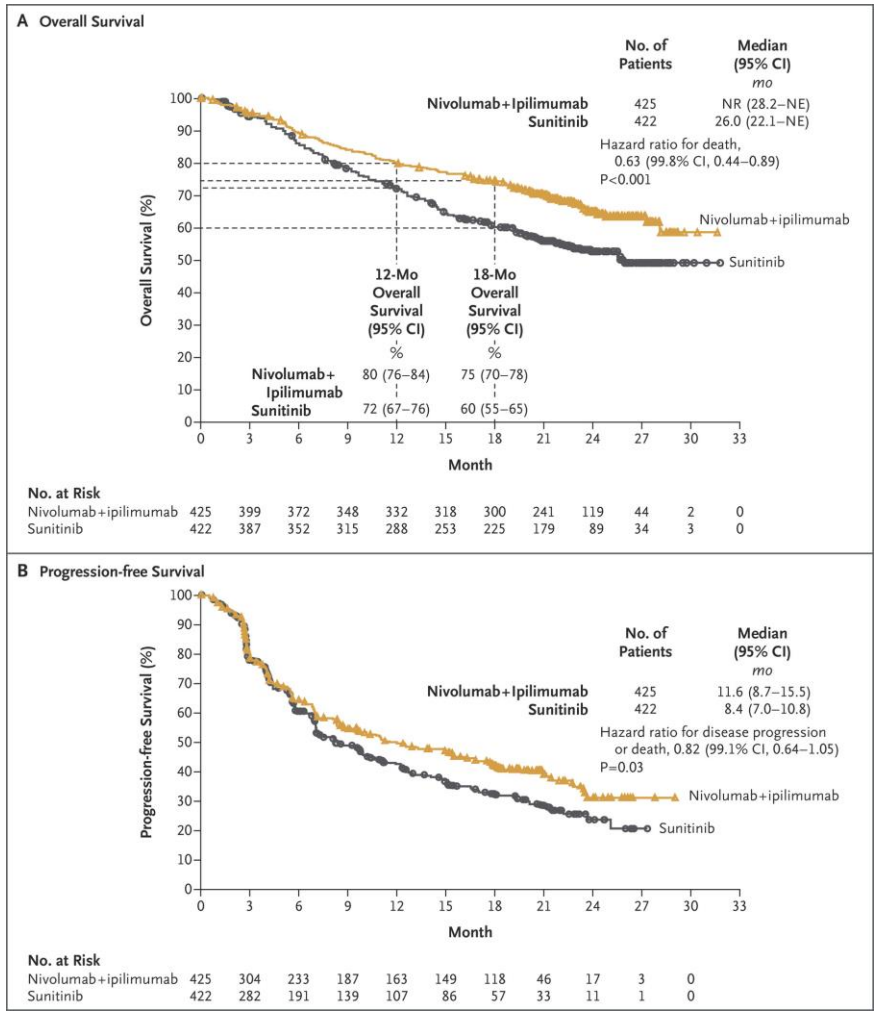
- Studie SURTIME (Bex et al., 2019)

# Změna přístupu – EAU Guidelines

| Recommendations | Strength rating |
|---|---|
| Do not perform cytoreductive nephrectomy (CN) in MSKCC poor-risk patients. | Strong |
| Do not perform immediate CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy. | Weak |
| Start systemic therapy without CN in intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy. | Weak |
| Discuss delayed CN with patients who derive clinical benefit from systemic therapy. | Weak |
| Perform immediate CN in patients with a good performance status who do not require systemic therapy. | Weak |
| Perform immediate CN in patients with oligometastases when complete local treatment of the metastases can be achieved. | Weak |

# Checkmate 214

- Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. N Engl J Med. 2018

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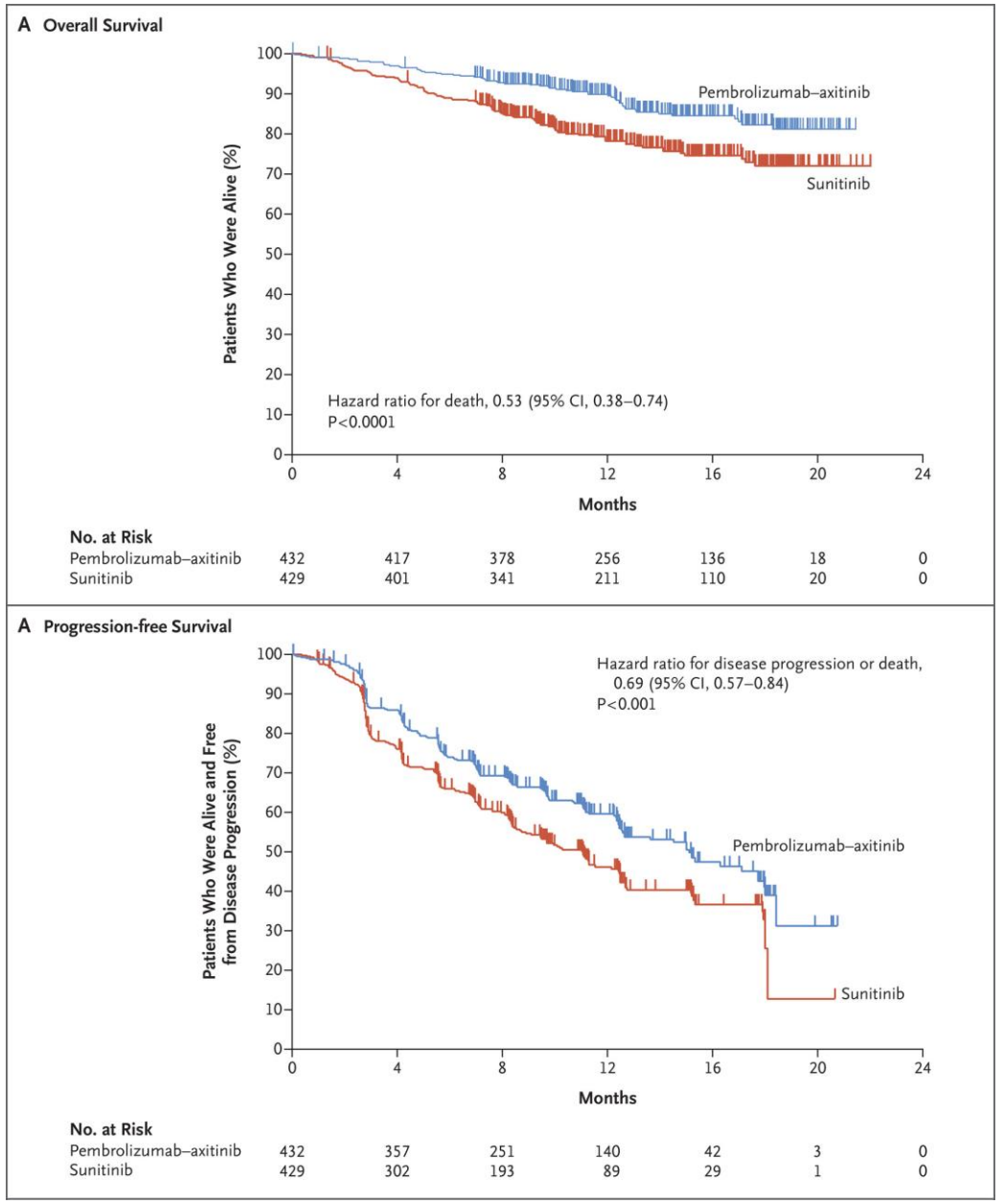
# Keynote 426

- Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med. 2019

- Pembro +Axitinib vs. Sunitinib

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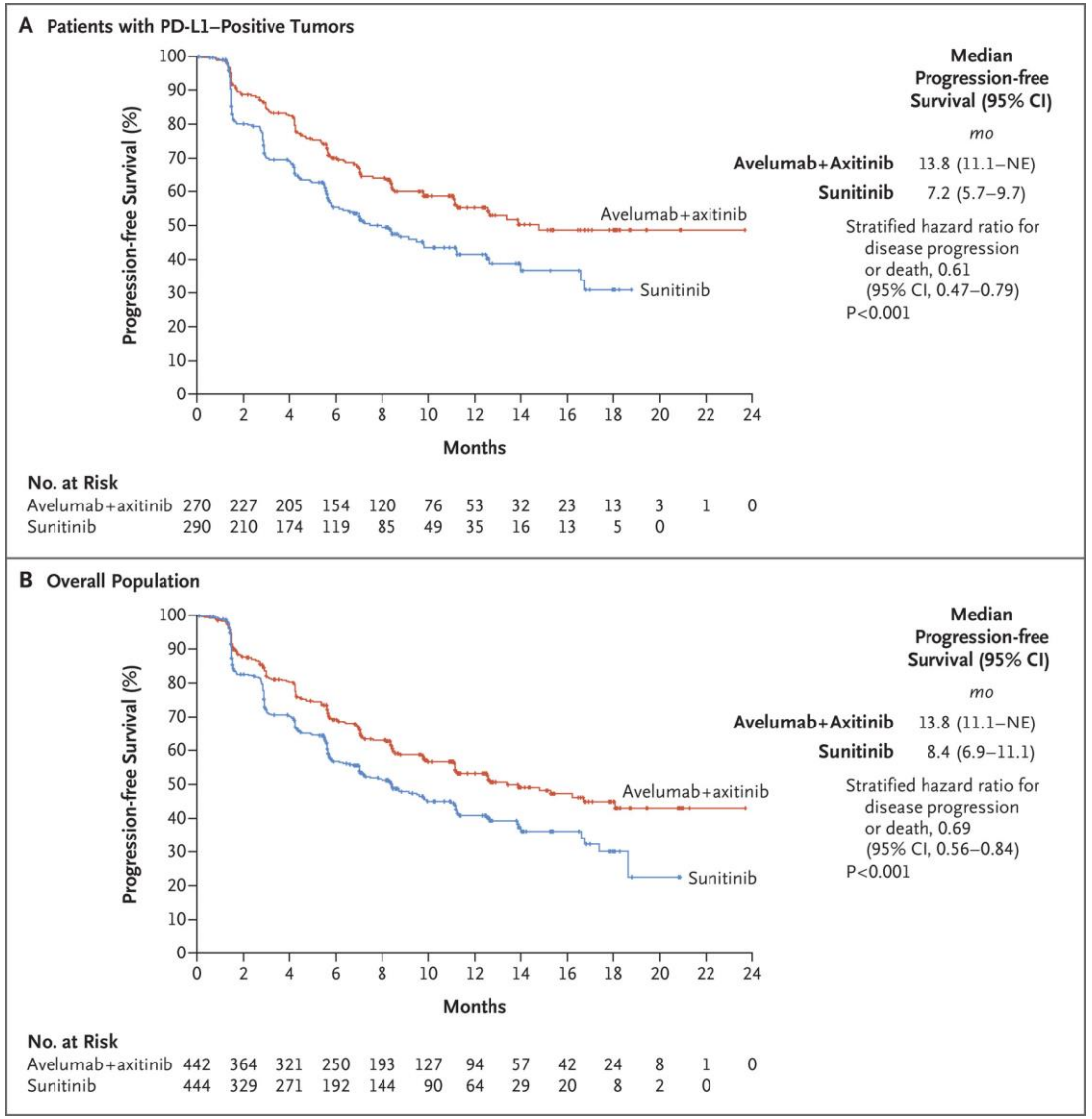
# Javelin 101

- Motzer RJ, Penkov K, Haanen J, et al. Avelumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med. 2019

- Avelumab +Axitinib vs. Sunitinib

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# EAU guidelines 2021

| | Standard of Care | Alternative in patients who can not receive or tolerate immune checkpoint inhibitors |
|---|---|---|
| IMDC favourable risk | nivolumab/cabozantinib [1b]<br>pembrolizumab/axitinib [1b]<br>pembrolizumab/lenvatinib [1b] | sunitinib* [1b]<br>pazopanib* [1b] |
| IMDC intermediate and poor risk | nivolumab/cabozantinib [1b]<br>pembrolizumab/axitinib [1b]<br>pembrolizumab/lenvatinib [1b]<br>nivolumab/ipilimumab [1b] | cabozantinib* [2a]<br>sunitinib*[1b]<br>pazopanib* [1b] |

# Morbidita cytoredukční nefrektomie

# IMDC

- Risk group stratification

| Risk factors** | Cut-off point used |
|---|---|
| Karnofsky performance status | < 80% |
| Time from diagnosis to treatment | < 12 months |
| Haemoglobin | < Lower limit of laboratory reference range |
| Corrected serum calcium | > 10.0 mg/dL (2.4 mmol/L) |
| Absolute neutrophil count (neutrophilia) | > upper limit of normal |
| Platelets (thrombocytosis) | > upper limit of normal |

~~0 factors: favourable-risk disease~~
1–2 factors: intermediate-risk disease
3–6 factors: poor-risk disease

# Mortality and Morbidity After Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma: A Population-Based Study

2011

Firas Abdollah, MD[1,2], Maxine Sun, BSc[1], Rodolphe Thuret, MD[1,3], Jan Schmitges, MD[1,4], Shahrokh F. Shariat, MD[5], Paul Perrotte, MD[1,6], Francesco Montorsi, MD[2], and Pierre I. Karakiewicz, MD[1,6]

| Complication | Overall (n = 17,688) (100.0%) | CNT (n = 1063) (6.0%) | NT (n = 16,625) (94.0%) | P value |
|---|---|---|---|---|
| In-hospital mortality | 180 (1.0) | 25 (2.4) | 155 (0.9) | <0.001 |
| In-hospital complications[a] | 3430 (19.4) | 282 (26.5) | 3148 (18.9) | <0.001 |
| Cardiac complications | 406 (2.3) | 42 (4.0) | 364 (2.2) | <0.001 |
| Respiratory complications (excluding pneumothorax) | 510 (2.9) | 36 (3.4) | 474 (2.9) | 0.3 |
| Pneumothorax | 315 (1.8) | 29 (2.7) | 286 (1.7) | 0.01 |
| Vascular complications | 182 (1.0) | 35 (3.3) | 147 (0.9) | <0.001 |
| Digestive system complications | 1086 (6.1) | 57 (5.4) | 1029 (6.2) | 0.2 |
| Urinary complications | 335 (1.9) | 18 (1.7) | 317 (1.9) | 0.6 |
| Accidental puncture or laceration during a procedure | 726 (4.1) | 71 (6.7) | 655 (3.9) | <0.001 |
| Hemorrhage/hematomas | 496 (2.8) | 56 (5.3) | 440 (2.6) | <0.001 |
| Seromas | 13 (0.1) | 2 (0.2) | 11 (0.1) | 0.1 |
| Operative wound complications | 22 (0.1) | 4 (0.4) | 18 (0.1) | 0.01 |
| Postoperative infections | 101 (0.6) | 6 (0.6) | 95 (0.6) | 0.9 |
| Transfusion | 2104 (11.9) | 258 (24.3) | 1846 (11.1) | <0.001 |

# Mortality and Morbidity After Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma: A Population-Based Study

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# Morbidity and Mortality of Radical Nephrectomy for Patients With Disseminated Cancer: An Analysis of the National Surgical Quality Improvement Program Database

2016

**Christopher J. D. Wallis, Georg Bjarnason, James Byrne, Douglas C. Cheung, Azik Hoffman, Girish S. Kulkarni, Avery B. Nathens, Robert K. Nam, and Raj Satkunasivam**

| | Nondisseminated n = 7143 | Disseminated n = 657 | Fisher's exact *P* Value |
|---|---|---|---|
| Major complication (n, %) | 229 (3.2) | 48 (7.3) | <.0001 |
| Mortality | 38 (0.5) | 21 (3.2) | <.0001 |
| Reoperation | 148 (2.1) | 26 (4.0) | .004 |
| Cardiac complication | 66 (0.9) | 11 (1.7) | .09 |
| Neurologic complication | 14 (0.2) | 2 (0.3) | .64 |
| Pulmonary complication (n, %) | 137 (1.9) | 28 (4.3) | .0003 |
| Infectious complication (n, %) | 417 (5.8) | 61 (9.3) | .0009 |
| Sepsis | 157 (2.2) | 29 (4.4) | .001 |
| Pneumonia | 104 (1.5) | 22 (3.4) | .0009 |
| Urinary tract infection | 105 (1.5) | 9 (1.4) | .99 |
| Surgical site infection (SSI) | 135 (1.9) | 18 (2.7) | .14 |
| Organ space SSI | 27 (0.4) | 8 (1.2) | .007 |
| Deep incisional SSI | 17 (0.2) | 2 (0.3) | .67 |
| Superficial SSI | 95 (1.3) | 9 (1.4) | .86 |
| Venous thromboembolism (n, %) | 83 (1.2) | 18 (2.7) | .002 |
| Deep vein thrombosis | 50 (0.7) | 9 (1.4) | .09 |
| Pulmonary embolism | 42 (0.6) | 10 (1.5) | .01 |
| Bleeding requiring transfusion (n, %) | 953 (13.3) | 202 (30.8) | <.0001 |
| Prolonged length of stay (n, %) | 2260 (31.6) | 295 (44.9) | <.0001 |

# Morbidity and Mortality of Radical Nephrectomy for Patients With Disseminated Cancer: An Analysis of the National Surgical Quality Improvement Program Database

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2016

„Nefrektomie při generalizovaném onemocnění je spojena s významně vyšší morbiditou i mortalitou“

| | Nondisseminated n = 7143 | Disseminated n = 657 | Fisher's exact *P* Value |
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# Cytoreductive Nephrectomy in Patients with Synchronous Metastases from Renal Cell Carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium

2014

*Daniel Y.C. Heng [a,*,†], J. Connor Wells [a,†], Brian I. Rini [b], Benoit Beuselinck [c], Jae-Lyun Lee [d], Jennifer J. Knox [e], Georg A. Bjarnason [f], Sumanta Kumar Pal [g], Christian K. Kollmannsberger [h], Takeshi Yuasa [i], Sandy Srinivas [j], Frede Donskov [k], Aristotelis Bamias [l], Lori A. Wood [m], D. Scott Ernst [n], Neeraj Agarwal [o], Ulka N. Vaishampayan [p], Sun Young Rha [q], Jenny J. Kim [r], Toni K. Choueiri [s]*

[a] Tom Baker Cancer Center, Calgary, Alberta, Canada; [b] Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA; [c] University Hospitals Leuven, Leuven, Belgium; [d] Asan Medical Center, Seoul, South Korea; [e] Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [f] Sunnybrook Odette Cancer Centre, Toronto, Ontario, Canada; [g] City of Hope Comprehensive Cancer Cente, Duarte, CA, USA; [h] BCCA Vancouver Cancer Centre, Vancouver, British Columbia, Canada; [i] Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan; [j] Stanford Medical Center, Stanford, CA, USA; [k] Aarhus University Hospital, Aarhus, Denmark; [l] Department of Clinical Therapeutics, National & Kapodistrian University, Athens, Greece; [m] Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, Canada; [n] London Regional Cancer Centre, London, Ontario, Canada; [o] University of Utah Huntsman Cancer Institute, Salt Lake City, UT, USA; [p] Karmanos Cancer Institute, Detroit, MI, USA; [q] Yonsei University College of Medicine, Seoul, South Korea; [r] Sidney Kimmel Comprehensive Cancer Center at John Hopkins University, Baltimore, MD, USA; [s] Dana-Farber Cancer Institute, Boston, MA, USA

„ Pacienti s předpokládanou délkou přežití < 12 měsíců nebo s 4 a více IMDC prognostickými faktory neprofitují z CN.“

# Závěr

- Pacient se špatnou prognózou neindikovat k CN
- U středního rizika výkon odložit dle efektu léčby
- V případě symptomatického tumoru individualizovaný přístup

- Indikace by měla vycházet z multidisciplinárních týmů