# Nierenzellkarzinom Zytoreduktive surgery Wann?

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## Cytoreduktive Nephrektomie im Zeitalter gezielter pharmakologischer Tumortherapie

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Landesklinikum St. Pölten, St. Pölten

Landesklinikum St. Pölten · Weill Cornell Medical College

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## Nierenzellkarzinom

- Inzidenz steigt um 2.5% jährlich (8-9 / 100 000)
- Metastasiertes Nierenzellkarzinom:
  - Bis zu 30% der Patienten metastasiert zum Zeitpunkt der Diagnose
  - ~20% der Patienten mit primär nicht metastasierten Tumor entwickeln Metastasen nach der Nephrektomie, Prognose ist schlecht
    - medianes Überleben : 6-10 Monate
    - 2-Jahres Überlebensrate: 10%-20%

Rini et.al. Lancet,2009,373;1119-1132

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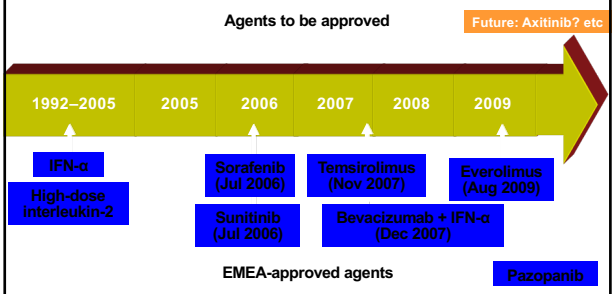
## Therapiefortschritte beim mRCC

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## Unterstützende Evidence für Cytoreduktive Nx

Zwei randomisierte Studien (EORTC and SWOG) publiziert im Jahr 2001 etablierten den Vorteil von cytoreduktive Nx plus Interferon vs. Interferon alleine.

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## Cytoreduktive Nephrektomie bei metastasierten RCC: Standard in der Cytokine Era

- Gefahrlos bei genau selektionierten Patienten
- Bietet Palliation für lokale Symptome
- Wirkung der Zytokine auf den Primärtumor minimal
- Verbesserung der Behandlungsergebnisse

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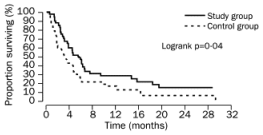
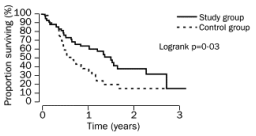
## EORTC 30947




Observed number of events / Number of patients at risk

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Study group | 32 | 42 | 23 | 12 | 10 | 7 | 4 | 2 | 1 |
| Controls | 37 | 42 | 17 | 8 | 5 | 2 | 1 | 1 | 1 |

Progressionsfreie Überlebenszeit




Observed number of events / Number of patients at risk

| | | | | | |
|---|---|---|---|---|---|
| Study group | 25 | 42 | 22 | 7 | 1 |
| Controls | 30 | 42 | 12 | 2 | 0 |

Gesamtüberleben

IFN + Nx 5 CR, 3 PR (19%)

IFN 1CR, 4 PR (12%)

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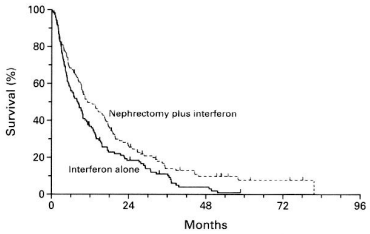
## SWOG 8949




IFN + Nx 3 PR (3%)

IFN 1 CR, 2 PR (4%)

No. at Risk

| | | | | | |
|---|---|---|---|---|---|
| Interferon alone | 121 | 21 | 4 | 0 | |
| Nephrectomy plus interferon | 120 | 29 | 9 | 3 | 0 |

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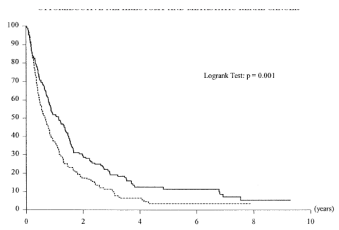
## EORTC/SWOG kombiniert




| O | N | Number of patients at risk : | | | | |
|---|---|---|---|---|---|---|
| 141 | 161 | 46 | 13 | 9 | 3 | Neph+IFN |
| 152 | 163 | 26 | 7 | 1 | 0 | IFN alone |

Fig. 1. Duration of survival in combined SWOG and EORTC trials. *O*, observation. *N*, nephrectomy

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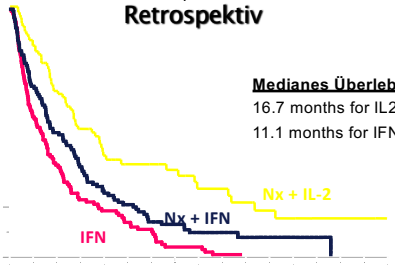
## 2001 SWOG vs. UCLA




**Medianes Überleben**
16.7 months for IL2 after Nx
11.1 months for IFN after Nx

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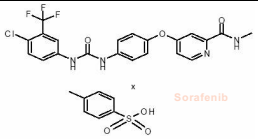
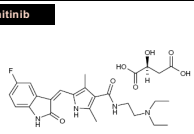
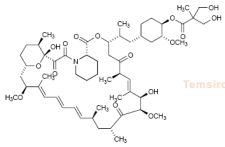



Was ist die Rolle von cytoreduktive Nephrektomie beim Einsatz von targeted therapy?

Rolle der TKI bei kurativer Nephrektomie?

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## Gründe für einen PARADIGMENWECHSEL?

- "bessere" systemische Therapie
- Neuere Biomarker - bessere Patientenselektion
- Morbidität des chirurgischen Eingriffs kann systemischen Ansatz verzögern/verhindern
- In Fallberichten gute Wirkung am Primärtumor
- Cytoreduktive Chirurgie ist nicht immer notwendig
  - Targeted Therapie behandelt alle tumorbefallenen Stellen
  - Nephrektomie verändert das Ergebniss nicht bei allen Patienten
  - Wir benötigen randomisierte Studien

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## Argumente für Cytoreduktive Nephrektomie

- Palliation von: Schmerz, Blutung, Paraneoplastisches Syndrom
- Primärtumor Hauptquelle für Metastasen
- Elimination von primärer Quelle von “Growth Factors und Immunosuppressiven Zytokinen”
- Primärer Tumor spricht nicht so gut auf systemische Therapie an
- Evtl. verzögert die Zeit bis zur Krankheitsprogression
- Evtl. verbessert Überleben
- Evtl. verbessert die Antwort auf systemische Therapie

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## Argumente gegen Cytoreduktive Nephrektomie

- Signifikante chirurgische Morbidität/Mortalität
- Einzig belegter Benefit in der Kombination mit IFN (“inferior” Therapie)
- Patient verbringt die meiste Überlebenszeit als Rekovaleszenz nach dem chirurgischen Eingriff
- Signifikante Krankheitsprogression während der post Op. Erholung kann die systemische Therapie ausschliessen
- Verzögerung der Initiation einer systemischen Therapie um die Metastasen zu behandeln

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## Cytoreduktive Nephrektomie bei metastasierten Nierenzellkarzinom

- Gefahrlos bei genau selektionierten Patienten
- Bietet Palliation für lokale Symptome
- Kein zuverlässiger Therapieeffekt von systemischer Therapie auf den primären Tumor
- Verbesserung der Behandlungsergebnisse

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## Patientenselektion für Cytoreduktive Nephrektomie

- ECOG Status 0-1
- Keine signifikanten Komorbiditäten
- Keine CNS, Leber-, ausgeprägte Knochen -metastasen
- Grosser Primärtumor/Fähigkeit den Großteil des Tumors in einer Sitzung zu entfernen
- Keine sarcomatoide Dedifferentierung
- Klarzellige Histologie

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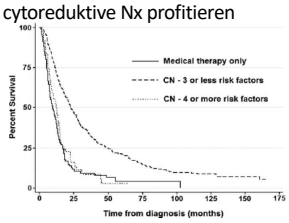
| | | | |
|---|---|---|---|
| **Serum albumin, g/dL** | | | |
| 3.5-4.7[a] | Referent | — | — |
| <3.5 | 1.59 | 1.21-2.10 | .001 |
| >4.7 | 1.18 | 0.28-4.86 | .823 |
| **Serum alkaline phosphatase, IU/L** | | | |
| 38-126[b] | Referent | — | — |
| >126 | 0.89 | 0.70-1.14 | .359 |
| **Serum lactate dehydrogenase, IU/L** | | | |
| 313-618[b] | Referent | — | — |
| <313 | 0.73 | 0.46-1.15 | .169 |
| >618 | 1.66 | 1.26-2.18 | <.001 |
| **Hemoglobin, g/dL** | | | |
| 14-18 (Men) or 12-16 (women)[b] | Referent | — | — |
| <12 (Men) or <14 (women) | 0.99 | 0.76-1.29 | .920 |
| >16 (Men) or >18 (women) | 1.00 | 0.24-4.25 | .999 |
| Metastasectomy at any time[c] | 0.92 | 0.75-1.14 | .458 |
| Liver metastasis | 1.47 | 1.02-2.13 | .039 |
| **Clinical tumor classification** | | | |
| T1 | Referent | — | — |
| T2 | 1.28 | 0.95-1.72 | .108 |
| T3 | 1.37 | 1.01-1.87 | .045 |
| T4 | 2.05 | 1.13-3.72 | .019 |
| Fuhrman nuclear grade | 1.19 | 1.01-1.40 | .041 |
| **No. of metastatic sites at CN[d]** | | | |
| 0-1 | Referent | — | — |
| 2-3 | 1.13 | 0.89-1.43 | .305 |
| ≥3 | 1.17 | 0.47-2.96 | .734 |
| Sarcomatoid dedifferentiation | 1.40 | 1.08-1.80 | .011 |
| Clear cell histology | 0.75 | 0.55-1.02 | .063 |
| **Symptoms at presentation** | | | |
| Metastatic symptoms | 1.35 | 1.03-1.75 | .028 |
| Systemic symptoms | 1.12 | 0.85-1.49 | .413 |
| Local symptoms | 1.14 | 0.89-1.46 | .306 |
| Laparoscopic nephrectomy | 1.04 | 0.73-1.50 | .816 |
| Retroperitoneal lymphadenopathy | 1.29 | 1.01-63 | .040 |
| Supradiaphragmatic lymphadenopathy | 1.48 | 1.18-1.86 | .001 |

## Patientenselektion für cytoreduktive Nephrektomie bei metastasiertem RCC

7 präoperative Risikofaktoren zum Zeitpunkt der initialen Evaluierung um die Patienten mit mRCC zu identifizieren, die von der cytoreduktive Nx profitieren




Shariat et al., in preparation

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## Cytoreduktive Nephrektomie bei metastasierten Nierenzellkarzinom

- Gefahrlos bei genau selektionierten Patienten
- Bietet Palliation für lokale Symptome
- Kein zuverlässiger Therapieeffekt von systemischer Therapie auf den primären Tumor
- Verbesserung der Behandlungsergebnisse

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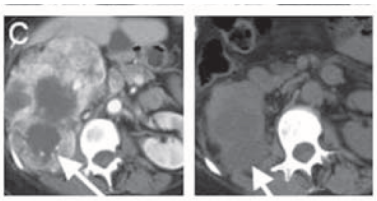
## Sunitinib bei metastasiertem RCC: Beispiel für Tumorreduktion



Prä-Therapie Post-Therapie

Motzer RJ et al. *J Clin Oncol*. 2006;24:1-8.

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## Behandlung mit Targeted Therapy kann nicht zur Heilung führen

- Keine verläßliche komplette Rückbildung
- Ohne extirpative/ablative Therapie (i.e. Chirurgie) kann niemand geheilt werden
  - Behandlungsziel muß immer Heilung sein

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## Cytoreduktive Nephrektomie bei metastasierten Nierenzellkarzinom

- Gefahrlos bei genau selektionierten Patienten
- Bittet Palliation für lokale Symptome
- Kein zuverlässiger Th. Effekt von systemische Th. Auf den primären Tumor
- Verbesserung der Behandlungsergebnisse

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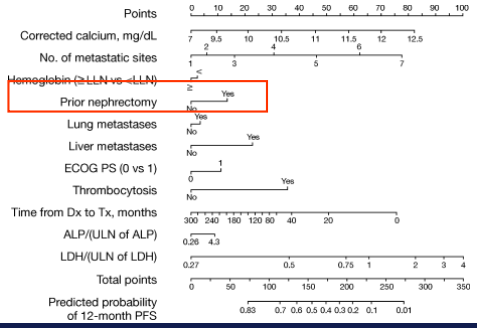
## Sunitinib Nomogram Predicting Probability of Progression-free Survival at 12-Months

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Motzer et al., Cancer 2008; 113:1552-8

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Die Frage ist nicht ob Chirurgie in der Behandlung von mRCC inkludiert werden soll, sondern *wann*?

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## Verzögerte Cytoreduktive Nephrektomie: *Pre*-chirurgische Behandlung

| PRO | KON |
|---|---|
| • Selektiert die Patienten für Chirurgie die auf syst. Therapie ansprechen | • Kann addieren zur chirurgischen morbidität/mortalität |
| • Down-staging erleichtert künftige Chirurgie | • Kann die Konditionen bei guten chirurgischen Kandidaten verschlechtern |
| • Eliminiert morbidität/mortalität bei allen die ohnehin keinen Benefit hätten | • Kein nachgewiesener Benefit |
| • Weniger toxisch als Therapie mit Zytokinen | • Anleitungspunkt nicht klar definiert |

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Shariat et al., BJUI 2008

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## Issues of *Pre*-surgical Approaches

- **Therapy may increase surgical morbidity and complications**
  - Potential for higher incidence of wound complications, peri-op bleeding and thromboembolic events
- **Local tumor progression in non-responders increases complexity of the surgery**
  - More "ectomies"= Worse outcome
- **Optimal time to proceed with Nx?**
  - Why interrupt a therapeutic response?
  - Who wants to operate on therapy refractory disease?

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## Neoadjuvant Sutent Induction Therapy May Effectively Down-Stage Renal Cell Carcinoma Atrial Thrombi

Fig. 1 – Pretreatment computed tomography scan demonstrates the left-sided primary tumor with a necrotic center and a massive renal vein and inferior vena cava thrombus with cephalad extension into the right atrium.

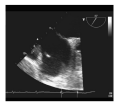

Fig. 2 – Cardiac echography demonstrating the protruding tumor thrombus within the right atrium. The broken arrow demonstrates the dimension of the intra-atrial aspect of the thrombus, which measured 1 × 2 cm.

Fig. 3 – A magnetic resonance image demonstrates the residual thrombus after two cycles of sunitinib. The thrombus consists of a solid component (dark filling defect at the ostium of the renal vein) and of a thin stalk that emanates from the proximal part of the renal vein.

Pre-surgical Sunitinib resulted in down-staging of tumor thrombus from right atrium to the infrahepatic portion of IVC

- avoidance of added morbidity of sternotomy

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Karakiewicz et al., Eur Urol 2008; 53:845-8

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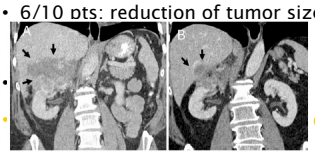
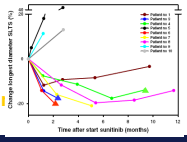
## Neoadjuvant sunitinib for surgically complex advanced renal cell cancer of doubtful resectability: initial experience with downsizing to reconsider cytoreductive surgery

- Retrospective analysis of 10 patients with complex metastatic RCC treated with initial sunitinib
- All had primary or retroperitoneal lesions with direct invasion of adjacent organs or encasement vital structures
- 6/10 pts: reduction of tumor size (median of 14%:



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Bex et al., World J Urol 2009

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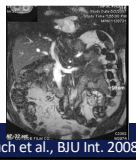
## Neoadjuvant targeted therapy and advanced kidney cancer: observations and implications for a new treatment paradigm

- Case series of 4 patients with metastatic RCC treated with initial sunitinib or sorafenib
- Response within primary tumor, tumor thrombus, renal fossa recurrence, and regional lymph node metastases
- Pre-surgical therapy was thought to **facilitate surgery in select patients with locally advanced RCC**

*FIG. 1. A level II IVC tumour thrombus at disease presentation.*

*FIG. 2. After neoadjuvant therapy, showing a level I IVC tumour thrombus.*



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Shuch et al., BJU Int. 2008 ;102(6):692-6

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## Nephrectomy for Metastatic RCC Remains the Standard of Care

- Without complete responses, surgery remains integral part of multi-disciplinary approach
  - Control of primary tumor
  - Metastasectomy
- Reliable complete responses with any agent will force re-examination of current paradigm
- Pre-surgical approach may have merit but needs further study and validation
  - Not clear when it is most appropriate to integrate surgery

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## Nephrectomy for Metastatic RCC in the Era of Targeted Therapy: Not a question of "if" but "when"? (cytoreductive vs consolidative)

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# CARMENA

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma

A. Méjean, A. Ravaud, S. Thezenas, S. Colas, J.-B. Beauval, K. Bensalah, L. Geoffrois, A. Thiery-Vuillemin, L. Cormier, H. Lang, L. Guy, G. Gravis, F. Rolland, C. Linassier, E. Lechevallier, C. Beisland, M. Aitchison, S. Oudard, J.-J. Patard, C. Theodore, C. Chevreau, B. Laguerre, J. Hubert, M. Gross-Goupil, J.-C. Bernhard, L. Albiges, M.-O. Timsit, T. Lebret, and B. Escudier



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# CARMENA

**CONCLUSIONS**

Sunitinib alone was not inferior to nephrectomy followed by sunitinib in patients with metastatic renal-cell carcinoma who were classified as having intermediate-risk or poor-risk disease. (Funded by Assistance Publique–Hôpitaux de Paris and others; CARMENA ClinicalTrials.gov number, NCT00930033.)



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# CARMENA

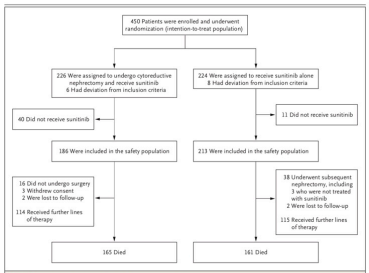


**Figure 1. Randomization, Treatment, and Follow-up of the Patients.**
The numbers of patients who died were based on the intention-to-treat population. The patients who did not undergo surgery (in the nephrectomy–sunitinib group) or who underwent subsequent nephrectomy (in the sunitinib-alone group), who withdrew consent, who were lost to follow-up, or who received further lines of therapy were all included in the analyses of overall survival and progression-free survival.



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**Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.***

| Characteristic | Nephrectomy–Sunitinib (N=226) | Sunitinib Alone (N=224) |
|---|---|---|
| Median age (range) — yr | 63 (33–84) | 62 (30–87) |
| Male sex — no. (%) | 169 (74.8) | 167 (74.6) |
| MSKCC risk category — no./total no. (%)† | | |
| Intermediate risk | 125/225 (55.6) | 131/224 (58.5) |
| Poor risk | 100/225 (44.4) | 93/224 (41.5) |
| ECOG performance-status score — no. (%)‡ | | |
| 0 | 130 (57.5) | 122 (54.5) |
| 1 | 96 (42.5) | 102 (45.5) |
| Fuhrman grade of renal-cell carcinoma — no./total no. (%)§ | | |
| 1 or 2 | 77/150 (51.3) | 82/156 (52.6) |
| 3 or 4 | 73/150 (48.7) | 74/156 (47.4) |
| Tumor–node–metastasis stage — no./total no. (%)¶ | 71/207 (34.3) | 50/194 (25.8) |
| Tumor stage | | |
| T1 | 5/67 (7.5) | 7/49 (14.3) |
| T2 | 13/67 (19.4) | 13/49 (26.5) |
| T3 or 4 | 47/67 (70.1) | 25/49 (51.0) |
| Tx | 2/67 (3.0) | 4/49 (8.2) |
| Node stage | | |
| N0 | 23/66 (34.8) | 18/49 (36.7) |
| N1 | 13/66 (19.7) | 6/49 (12.2) |
| N2 | 7/66 (10.6) | 13/49 (26.5) |
| Nx | 23/66 (34.8) | 12/49 (24.5) |
| Median primary tumor size (range) — mm | 88 (6–200) | 86 (12–190) |
| Median no. of metastatic sites (range) | 2 (1–5) | 2 (1–5) |
| Median tumor burden (range) — mm‖ | 140 (23–399) | 144 (39–313) |
| Location of metastases — no./total no. (%) | | |
| Lung | 172/217 (79.3) | 161/221 (72.9) |
| Bone | 78/217 (35.9) | 82/221 (37.1) |
| Lymph nodes | 76/217 (35.0) | 86/221 (38.9) |
| Other | 78/217 (35.9) | 90/221 (40.7) |

* The characteristics of the patients at baseline were well balanced between the treatment groups.
† The Memorial Sloan Kettering Cancer Center (MSKCC) prognostic factors regarding oral-oxen-y Karnofsky performance status score of less than 80 (on a scale from 0 to 100, with lower scores indicating greater disability), a lactate dehydrogenase level of 1.5 times the upper limit of the normal range, a hemoglobin level that was less than the lower limit of the normal range, a corrected serum calcium level of more than 10 mg per deciliter (2.5 mmol per liter), and a time from diagnosis to treatment of less than 1 year. Patients with zero or one of these factors were classified as having intermediate-risk disease and those with three or more were classified as having poor-risk disease.
‡ Eastern Cooperative Oncology Group (ECOG) performance-status scores range from 0 to 5, with higher scores indicating greater disability. Scores of 5 indicate death.
§ The Fuhrman grade of renal-cell carcinoma is assessed on a scale of 1 to 4, with grade 1 indicating the least atypia and grade 4 the most.
¶ The tumor–node–metastasis stage was determined according to the criteria of the Union for International Cancer Control TNM Classification of Malignant Tumours.[9] Metastasis was an eligibility criterion in all patients.
‖ Tumor burden was assessed according to the Response Evaluation Criteria in Solid Tumors, version 1.1.



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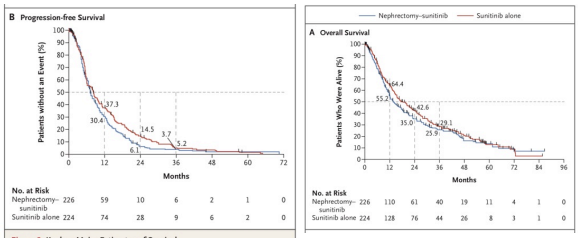


**Figure 2. Kaplan–Meier Estimates of Survival.**
The landmark analyses of overall survival (Panel A) and progression-free survival (Panel B) at 1, 2, and 3 years are indicated by the vertical dashed lines, with rates in the two groups shown at those time points. The horizontal dashed line in each panel indicates the median. Tick marks indicate censored data.



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# CARMENA Diskussions-/Kritikpunkte

1. Diese Studie wurde für die langsame und unvollständige Rekrutierung kritisiert

- In 8 Jahren wurden 450 Patienten an 79 internationalen Zentren inkludiert (geplant waren 576 Patienten)

➢ Steigende Möglichkeiten für „Rekrutierungs bias“

Wurden Patienten mit geringer ausgeprägtem Metastasierungsmuster außerhalb der Studie behandelt?



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## CARMENA Diskussions-/Kritikpunkte

1. OS Differenzen verglichen mit der rezenten Studie, die bei ähnlichem Patientengut publiziert wurde

- The median OS of CN versus non-CN patients was 17.1 (95% CI, 16.3 to 18.0 months) versus 7.7 months (95% CI, 7.4 to 7.9 months; $P < .001$)

Hanna N, Sun M, Meyer CP, et al. Survival analyses of patients with metastatic renal cancer treated with targeted therapy with or without cytoreductive nephrectomy: a National Cancer Data Base study. J Clin Oncol 2016;34:3267–75.

➢ In both the intermediate-risk and poor-risk groups of patients, the median overall survival was longer in the sunitinib-alone group than in the nephrec- tomy–sunitinib group (23.4 vs. 19.0 months in the intermediate-risk subgroup and 13.3 vs. 10.2 months in the poor-risk group).

Méjean A, Ravaud A, Thezenas S, et al. Sunitinib alone or after nephrectomy in metastatic renal-cell carcinoma. N Engl J Med 2018;379:417–27



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## CARMENA Diskussions-/Kritikpunkte

1. Die Generalisierbarkeit dieser Studie ist in der populationsbasierten Datenbank nicht beurteilt worden

- Randomization was stratified according to risk group (classified according to the Memorial Sloan Kettering Cancer Center [MSKCC] prognostic model).

Méjean A, Ravaud A, Thezenas S, et al. Sunitinib alone or after nephrectomy in metastatic renal-cell carcinoma. N Engl J Med 2018;379:417–27

➢ CARMENA Patienten sind nicht bedingungslos projizierbar auf die Praxis und weisen ein ausgeprägteres Metastasierungsmuster auf, als durchschnittliches Patientengut. Es kann impliziert werden, dass die Patienten mit geringer ausgeprägtem Metastasierungsmuster außerhalb der Studie eine Nephrektomie erhielten.



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## CARMENA Diskussions-/Kritikpunkte

**Table 1 – Descriptive statistics for 450 patients randomized to receive sunitinib or a combination of cytoreductive nephrectomy and sunitinib in the CARMENA trial compared with 2800 patients with similar inclusion/exclusion criteria, treated with cytoreductive nephrectomy between 2010 and 2015, in the NCDB**

| Variable | NCDB cohort (n = 2800) | CARMENA trial (n = 450) | p value [c] |
|---|---|---|---|
| Median age (yr) | 60 (IQR 53–67) | 62.5 (range 30–87) | – |
| Median tumor size (mm) | 91 (IQR 70–120) | 87 (range 6–200) | – |
| Median number of metastatic sites | 1 (IQR 1–2; range 1–4) | 2 (range 1–5) | – |
| Gender, male n (%) | 1960 (70) | 336 (75) | <0.001 |
| Fuhrman grade, n (%) [b] | | | <0.001 [c] |
| Grade 1 or 2 | 501 (18) | 159/306 (52) | |
| Grade 3 or 4 | 2143 (77) | 147/306 (48) | |
| Missing | 156 (6) | – | |
| T stage, n (%) [d] | | | <0.001 [c] |
| T1 | 258 (9) | 12/116 (10) | |
| T2 | 417 (15) | 26/116 (22) | |
| T3/T4 | 2022 (72) | 72/116 (62) | |
| Missing/Tx | 103 (4) | 6/116 (0.1) | |
| Site of metastases, n (%) [e] | | | |
| Lung | 1726 (62) | 172/217 (79) | <0.001 |
| Bone | 839 (30) | 78/217 (36) | <0.001 |
| Lymph node | 723 (26) | 76/217 (35) | <0.001 |
| Other | 366 (13) | 168/438 (38) | 0.3 |

NCDB = National Cancer Data Base; IQR = interquartile range.
[a] A $\chi^2$ test was used to test the statistical significance of differences in categorical variables. Since measures of variance were not available for the trial cohort, it was not possible to calculate p values for continuous variables. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA), with a $p < 0.05$ considered significant.
[b] Grade and information available for 306 patients in CARMENA.
[c] Missing values were not included in the analysis for significance.
[d] T stage information available for 116 patients in CARMENA. Trial data derived from clinical, paraclinical, biological, and anatomopathology information.
[e] Derived from clinical information on location of metastases in both CARMENA and NCDB.

Sohrab Arora a, Akshay Sood a, Deepansh Dalela a, Hoang J. Tang a, Amit Patel a, Jacob Keeley a, Quoc-Dien Trinh b, Craig G. Rogers a, Mani Menon a, Firas Abdollah a, Eur. Urol. 2018



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The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

**Cytoreductive Nephrectomy — Patient Selection Is Key**

Robert J. Motzer, M.D., and Paul Russo, M.D.

MotzerRJ,RussoP.Cytoreductivenephrectomy—patientselectionis key. N Engl J Med 2018;379:481–2.



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- In the CARMENA trial, 43% of the patients had poor-risk disease and the remaining patients had intermediate-risk disease. The nephrectomy– sunitinib group had a higher percentage of locally advanced tumors of stage T3 or T4 than the sunitinib group (70.1% vs. 51.0%), which could have affected surgical outcomes.
- The survival among patients who were enrolled in the CARMENA trial reflects the selected population of patients. The median over-all survival was 13.9 months (95% confidence interval [CI], 11.8 to 18.3) in the nephrectomy– sunitinib group and 18.4 months (95% CI, 14.7 to 23.0) in the sunitinib-alone group.
- By comparison, in two recent randomized, controlled trials in which sunitinib was compared with other regimens in intermediate-risk and poor- risk patients, the median overall survival in the sunitinib-only group was 26.0 months (95% CI, 22.1 to could not be estimated) in one trial and 21.8 months (95% CI, 16.3 to 27) in the other.

MotzerRJ,RussoP.Cytoreductivenephrectomy—patientselectionis key. N Engl J Med 2018;379:481–2.



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## ASCO 2019: Update on the CARMENA Trial with focus on Intermediate IMDC risk Population

Aktualisierung der Studienergebnisse unter Verwendung des IMDC-Scores und eines verlängerten Nachbeobachtungszeitraums (61,5 Monate)

Betrachtete man Patienten mit lediglich einem Risikofaktor ergab sich nun ein signifikanter Überlebensvorteil (OS) zugunsten der CN (31,4 vs. 25,2 Monate; HR=1,29)

Presented by: Arnaud Mejean at the 2019 ASCO Annual Meeting, Chicago IL USA



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## ASCO 2019: Update on the CARMENA Trial with focus on Intermediate IMDC risk Population

Ein Vorteil für die CN zeigte sich bei den Patienten mit:

- nur einer Metastase (23,2 vs. 14,$ Monate)
- Mit lediglich Lungenmetastasen (44 vs. 31,5 Monate)

Presented by: Arnaud Mejean at the 2019 ASCO Annual Meeting, Chicago IL USA

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## ASCO 2019: Update on the CARMENA Trial with focus on Intermediate IMDC risk Population

- Ein weiterer Überlebensvorteil zeigte sich bei Patienten , die zunächst Sunitinib erhielten und bei gutem Ansprechen im weiteren Verlauf nephrektomiert wurden.

Presented by: Arnaud Mejean at the 2019 ASCO Annual Meeting, Chicago IL USA

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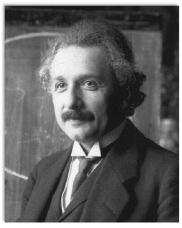
## Oversimplification

"Make things as simple as possible --- no simpler"

Albert Einstein



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