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Original Scientific Paper

EFFECTS OF TREATMENT WITH TEMSIROLIMUS *VERSUS* INTERFERON ALPHA ON SURVIVAL OF PATIENTS WITH METASTATIC RENAL CELL CARCINOMA – SINGLE-CENTER REAL-WORLD EXPERIENCE

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SUMMARY – Vascular endothelial growth factor (VEGF) and mammalian target of rapamycin (mTOR) inhibitors are two main groups of drugs for targeted treatment of metastatic renal cell carcinoma (mRCC). Inhibition of angiogenesis and other growth pathways that are pivotal for tumor progression lead to significant improvement of survival in patients with mRCC. The main aim of this study was to compare the effects of temsirolimus (mTOR inhibitor) and interferon alpha-2a (IFN-alpha-2a) on overall survival (OS) and progression-free survival (PFS) in patients with T3 stage mRCC who developed lung metastasis in the first two years after radical nephrectomy. A total of 60 patients diagnosed with T3 stage renal cancer who developed metastases in the lungs within two years after radical nephrectomy were included in a prospective study conducted at the Department for Urology, Clinical Center of Vojvodina and partially retrospective study at the Oncology Institute in Sremska Kamenica. Patients were divided into two groups consisting of 30 patients according to treatment with temsirolimus or IFN-alpha. During the first year of treatment, OS of patients treated with temsirolimus was 23.33%, whereas in patients treated with IFN-alpha it was 16.67%. Median survival in patients treated with temsirolimus was 9.3 months, whereas in patients treated with IFN-alpha it was 6.9 months, yielding a statistically significant difference (p=0.028). Patients treated with temsirolimus showed a statistically significantly longer median PFS compared to patients treated with IFN-alpha (p<0.0085). In conclusion, temsirolimus therapy had a significantly positive effect on survival in patients with mRCC. Patients treated with temsirolimus showed significantly longer median survival and median PFS compared to patients treated with IFN-alpha.

Keywords: *Renal cell carcinoma; Temsirolimus; Interferon alpha; Survival*

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Introduction

Renal cell carcinoma (RCC) is a heterogeneous malignant disease characterized by different histologic subtypes, genetic-molecular changes, disease course, and response to systemic therapy[1-3]. Over 30% of patients develop distant metastasis after radical nephrectomy[4,5]. On average, total survival of untreated patients with metastatic renal cell carcinoma (mRCC) is one year, whereas the five-year survival rate is just below 10%, which is indicative of mRCC aggressiveness[6,7]. Previously, the only option for systemic treatment of patients with mRCC was immunotherapy with cytokines, interleukin-2, and interferon alpha-2a (IFN-alpha-2a). Patients in the metastatic stages of the disease with poor prognostic factors seldom benefit from immunotherapy given its toxicity and limited therapeutic efficiency[8].

The introduction of a new generation of drugs that target intracellular molecular pathways included in the development, progression and metastasis of the malignant disease was revolutionary[9]. Inhibitors of the vascular endothelial growth factor (VEGF) and mammalian target of rapamycin (mTOR) are the two main drug classes of targeted therapy. By inhibiting angiogenesis and growth factor pathways which are essential for the progression of mRCC, targeted drugs induce significant improvements in outcomes of patients with mRCC[10]. mTOR is an intracellular serine/threonine kinase that plays a pivotal role in the regulation of angiogenesis, cell growth and metabolism as a response to external factors. Blocking the mTOR signaling pathway suppresses the production of the proteins that regulate the progression of the cell cycle and angiogenesis[11]. Temsirolimus is one of the two commercially available mTOR inhibitors, which has been approved for the treatment of patients with mRCC based on Level I evidence that it increases overall survival (OS) in low-risk patients[12-14].

The main aim of this study was to compare the effects of IFN-alpha and temsirolimus on OS and progression-free survival (PFS) in patients with T3 stage RCC who developed lung metastasis in the first two years of radical nephrectomy.

Patients and Methods

The research was conducted as a controlled, open, prospective and randomized study at the Department of Urology, Clinical Center of Vojvodina in Novi Sad and as partly retrospective study at the Oncology Institute of Vojvodina in Sremska Kamenica. A total of 60 patients diagnosed with T3 stage RCC who developed lung metastasis within two years of radical nephrectomy at the Department of Urology, Clinical Center of Vojvodina were included in the study. Patients were treated and monitored at the Oncology Institute in Sremska Kamenica and divided into two groups, i.e., test group and control group. The test group included 30 patients who were treated with temsirolimus, an mTOR inhibitor, whereas control group consisted of 30 patients in the same stage of the disease treated with immunotherapy (IFN-alpha-2a). The criteria for including patients in the study were as follows: age 18 to 65, T3 stage RCC, prior radical nephrectomy, verified metastasis in the lungs, and signed consent of patients to be included in the study. Excluding criteria were age over 65, metastasis in other organs, and inoperable RCC.

All procedures conducted as part of this study were compliant with ethical standards set by the Ethics Committee of the responsible institution (no. 00-08/103). Informed consent was obtained from each individual patient included in the study.

Therapeutic protocol of treatment with mTOR inhibitors involved administering 25 mg of temsirolimus intravenously over 30 minutes once a week. To prevent allergic reaction, patients were administered chloropyramine hydrochloride (20 mg/2 mL intravenously) half an hour after starting the treatment. The immunotherapy protocol consisted of administering IFN-alpha-2a three times a week, single dose of 6 million IU subcutaneously until reaching the total dose of 180 million IU. After a 4- to 6-week break, the therapeutic protocol was repeated until progression or unacceptable toxicity. Medical history of each patient included in the study was taken and clinical examination was performed. Prior to starting treatment, patients underwent chest x-ray, ultrasound of upper abdomen and kidneys, as well as blood tests including erythrocyte sedimentation rate, whole blood count, glycemia, urea, creatinine, uric acid, and electrolytes.

Diagnostic protocol included blood tests on day 3 of treatment each week, ultrasound of the upper abdomen and kidney every month (computed tomography scan if needed and indicated), chest x-ray every three months (computed tomography scan of the chest in case of significant changes on previous x-ray). All side effects and reactions were monitored, as well as general wellbeing of each patient during the study. PFS was assessed and defined as the time from the initiation of therapy to the day tumor progression was proven or death occurred. The patients were censored on the date of the last follow-up. OS was investigated from the initiation of therapy to the time of death as a result of any cause or censored on the date of the last follow-up.

Data collected during the study were stored in a specially created database. After entry, data processing included descriptive and inferential statistics. For all numerical parameters, we calculated arithmetic mean, standard deviation, coefficient of variation, and value range (minimal and maximal values). For all attributive parameters, frequency tables, i.e., contingency tables, were done in case of two parameters. Comparison of median values between the two groups was performed using Student's t-test. For comparison of proportions, z-test was used. For testing dependence of the parameter, the independence test was used, whereas survival analysis included Kaplan-Meier curve and logrank test. Statistical processing was performed *via* a software package, Statgraphics Centurion.

Results

During treatment, seven patients from the temsirolimus (test) group and five patients from the IFN-alpha-2a (control) group survived the first year of systemic therapy. OS during the first year of treatment was 23.33% in patients treated with temsirolimus and 16.67% in patients treated with IFN-alpha (Table 1).

Median OS was 9.27 months in the test group and 6.97 months in the control group. Patients treated with temsirolimus had a significantly longer median OS compared to patients treated with immunotherapy (p=0.0281). Median OS was expressed by the Kaplan-Meier curve (Fig. 1).

During the first year of treatment, the median progression-free time was 2.44 months in the control group and 3.696 months in the test group. Comparison of the results obtained in the study groups by Wilcoxon test revealed that patients treated with temsirolimus had a statistically significantly longer progression-free time (p=0.0084).

Discussion

Renal cell carcinoma is the most frequent type of renal malignancy; it accounts for 2%-3% of all malignancies in adults. Approximately 30% of new RCC cases present with advanced or metastatic disease

Table 1. Treatment effects on survival and PFS of patients during the first year of therapy

	Test group	**Control group**
Survived patients	7/30 (23.33%)	5/30 (16.67%)
Deceased patients	23/30 (76.67%)	25/30 (83.33%)
Mean survival time (months)	9.267	6.967
95% CI	7.732-10.172	4.537-7.888
Statistical difference for survival	p=0.0281	
PFS (months)	3.696	2.440
95% CI	2.932-4.459	2.241-2.639
Statistical difference for PFS	p=0.0085	

CI = confidence interval; PFS = progression-free survival

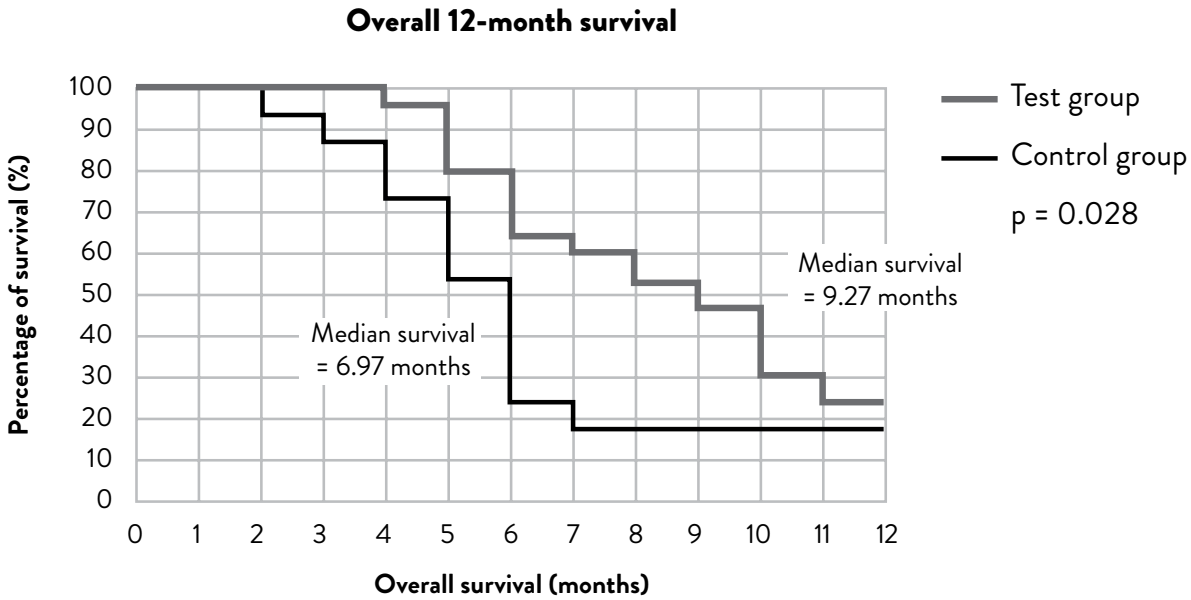

Fig. 1. Overall and median 12-month survival in test group and control group patients.

(mRCC) and the 5-year survival rate with mRCC is 5% to 10%[15]. Taking this into consideration, great efforts have been made over the past two decades and different treatment modalities have been developed for treatment of patients with mRCC[16]. Until 16 years ago, mRCC was treated using immunotherapeutic drugs, i.e., interleukin 2 and IFN-alpha with high toxicity and limited OS of about 13 months[17]. Through better understanding of the pathogenesis, especially tumor angiogenesis of RCC, new therapeutic agents have been developed such as VEGF and mTOR inhibitors[18].

The aim of this study was to compare the effects of immunotherapy and mTOR inhibitors on survival in patients with lung metastasis of RCC and poor prognostic factors. Patients with poor prognostic factors are those who have three or more of the following factors: Karnofsky performance status 60 or more, less than a year from diagnosis to randomization, hemoglobin values below minimum, corrected calcium higher than 10 mg/dL (2.5 mmol/L), lactate dehydrogenase ≥1.5 times above the upper limit of normal, and more than one metastatic hot spot. The first five factors belong to the Memorial Sloan-Kettering Cancer Center (MSKCC) classification system[19]. It is noteworthy that there are some disagreements on how to correctly identify patients with poor prognostic factors due to different criteria available in the most commonly used models of risk assessment such as MSKCC and Heng criteria[20]. It is extremely important to properly stratify the risks in those suffering from mRCC in order to choose appropriate systemic therapy. According to the latest guidelines of the Japanese Urological Association, National Comprehensive Cancer Network and European Medical Society of Oncology, temsirolimus is the first-line treatment for patients with mRCC and poor prognostic factors[21-23]. Additionally, results of multiple studies have shown that temsirolimus has proved to be efficient as second- and third-line mRCC therapy[24]. According to the results of the case study conducted by Satoh *et al.*[25], a patient who did not respond to therapy with tyrosine kinase inhibitors (sunitinib and axitinib) as first-line treatment was treated with temsirolimus and achieved complete remission of lung metastases during three years of treatment[25]. Unlike temsirolimus, systemic immunotherapy showed relatively good results only in patients with good prognostic factors.

Temsirolimus has proved to be efficient in treating both clear cell and other histologic types of RCC, unlike immunotherapy with cytokines which shows relatively satisfactory results only in patients with clear cell RCC[26]. This is supported by the results of the study on 44 patients with metastatic non-clear cell RCC treated with temsirolimus, where 3 (9%) patients achieved complete response, one (3%) patient had partial response, and in 25 (70%) patients the disease was stable during treatment, with overall response rate (ORR) of 11% and disease control rate (DCR) of 83%. In addition, the duration of good therapeutic response in all four patients was at least 15 months, which further supports the good and relatively lasting therapeutic efficiency of temsirolimus[26]. In our patient cohort, 7 (23.33%) patients were alive after 12 months *versus* 5 (16.67%) patients in the control group. After 6 months of therapy, 24 (80%) and 16 (53.33%) patients were still alive in the test group and control group, respectively.

When considering median OS in months, the mean OS was 9.267 months in the test group and 6.967 months in the control group, which implies a statistically significant longer survival in favor of temsirolimus. Results of a study published in 2019 show longer median survival in patients treated with temsirolimus in comparison with our results (mOS=17.6)[26]. Prolonged survival could be explained by the lower number of patients (n=44) and longer monitoring period (4 years). Results of another study published in 2017 show approximately the same median OS (mOS=10.4 months) as in our study (mOS=9.27 months)[27].

Important domain of our research was focused on the time elapsed from the start of treatment to the signs of progression, i.e., increase of recorded metastases in the lungs and appearance of new metastases in the lungs and other organs. Median PFS of patients was 3.7 months in the temsirolimus group, which was statistically significantly longer in comparison to 2.44 months recorded in the IFN-alpha-2a group. Considering median PFS, the results of our study are in concordance with the results reported by other researchers[26,27].

Conclusion

Temsirolimus therapy has a significantly positive effect on survival in patients with mRCC. Patients treated with temsirolimus showed significantly longer median OS and median PFS compared to patients treated with IFN-alpha.

References

1. Kovacs G, Akhtar M, Beckwith BJ, Bugert P, Cooper CS, Delahunt B, *et al*. The Heidelberg classification of renal cell tumours. J Pathol. 1997;183(2):131-3. PMID: 9390023 doi: 10.1002/(SICI)1096-9896(199710)183:2<131::AID-PATH931>3.0.CO;2-G
2. Moch H, Humphrey PA, Ulbright TM, Reuter VE. WHO Classification of Tumours of the Urinary System and Male Genital Organs – WHO Classification of Tumours, 4th ed.; WHO, Geneva; IARC Press, Lyon: 2016; Volume 8.
3. Theodoropoulos G, Tsiambas E, Tziakou P, Spyropoulou D, Niotis A, *et al*. MicroRNA signatures landscape in renal cell carcinoma-related epithelial to mesenchymal transition. JBUON. 2021;26(6):2209-12. ISSN: 1107-0625, online ISSN: 2241-6293.
4. Capitanio U, Montorsi F. Renal cancer. Lancet. 2016 Feb 27;387(10021):894-906. doi: 10.1016/S0140-6736(15)00046-X. Epub 2015 Aug 25. PMID: 26318520.
5. Mattila KE, Vainio P, Jaakkola PM. Prognostic factors for localized clear cell renal cell carcinoma and their application in adjuvant therapy. Cancers (Basel). 2022 Jan 4;14(1):239. doi: 10.3390/cancers14010239. PMID: 35008402; PMCID: PMC8750145.
6. Motzer RJ, Mazumdar M, Bacik J, Berg W, Amsterdam A, Ferrara J. Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. J Clin Oncol. 1999 Aug;17(8):2530-40. doi: 10.1200/JCO.1999.17.8.2530. PMID: 10561319.
7. Kubota S, Yoshida T, Kageyama S, Isono T, Yuasa T, Yonese J, Kushima R, Kawauchi A, Chano T. A risk stratification model based on four novel biomarkers predicts prognosis for patients with renal cell carcinoma. World J Surg Oncol. 2020 Oct 22;18(1):270. doi: 10.1186/s12957-020-02046-9. PMID: 33092599; PMCID: PMC7584101.
8. Mekhail TM, Abou-Jawde RM, Boumerhi G, Malhi S, Wood L, Elson P, Bukowski R. Validation and extension of the Memorial Sloan-Kettering prognostic factors model for

survival in patients with previously untreated metastatic renal cell carcinoma. J Clin Oncol. 2005 Feb 1;23(4):832-41. doi: 10.1200/JCO.2005.05.179. PMID: 15681528.

9. Del Bufalo D, Ciuffreda L, Trisciuoglio D, Desideri M, Cognetti F, Zupi G, Milella M. Antiangiogenic potential of the mammalian target of rapamycin inhibitor temsirolimus. Cancer Res. 2006 Jun 1;66(11):5549-54. doi: 10.1158/0008-5472.CAN-05-2825. PMID: 16740688.
10. Abdilkerim O, Melike O, Mustafa B, Ali G, Yildirim ME. First-line pazopanib in metastatic renal cell carcinoma: multicenter experience. JBUON. 2021;26(6):2581-6. ISSN: 1107-0625,online ISSN: 2241-6293.
11. Faes S, Demartines N, Dormond O. Mechanistic target of rapamycin inhibitors in renal cell carcinoma: potential, limitations, and perspectives. Front Cell Dev Biol. 2021 Mar 15;9:636037. doi: 10.3389/fcell.2021.636037. PMID: 33791295; PMCID: PMC8005589.
12. Kobayashi Y, Yamada D, Kawai T, Sato Y, Teshima T, Yamada Y, *et al*. Different immunological effects of the molecular targeted agents sunitinib, everolimus and temsirolimus in patients with renal cell carcinoma. Int J Oncol. 2020 Apr;56(4):999-1013. doi: 10.3892/ijo.2020.4975. Epub 2020 Feb 4. PMID: 32319571.
13. Cao G, Wu X, Wang Z, Tian X, Zhang C, Wu X, Zhang H, Jing G, Yan T. What is the optimum systemic treatment for advanced/metastatic renal cell carcinoma of favourable, intermediate and poor risk, respectively? A systematic review and network meta-analysis. BMJ Open. 2020 Aug 27;10(8):e034626. doi: 10.1136/bmjopen-2019-034626. PMID: 32859659; PMCID: PMC7454197.
14. Levakov I, Vojinov S, Marusic G, Popov M, Levakov O, Popov M, Jeremic D. Safety profile of temsirolimus in patients with metastatic renal cell carcinoma. JBUON. 2016 Nov-Dec;21(6):1442-8. PMID: 28039705.
15. Bosma NA, Warkentin MT, Gan CL, Karim S, Heng DYC, Brenner DR, Lee-Ying RM. Efficacy and safety of first-line systemic therapy for metastatic renal cell carcinoma: a systematic review and network meta-analysis. Eur Urol Open Sci. 2022 Jan 22;37:14-26. doi: 10.1016/j.euros.2021.12.007. PMID: 35128482; PMCID: PMC8792068.
16. Escudier B, Albiges L, Sonpavde G. Optimal management of metastatic renal cell carcinoma: current status. Drugs. 2013 Apr;73(5):427-38. doi: 10.1007/s40265-013-0043-1. PMID: 23572408.
17. Schwab M, Hofmann R, Heers H, Hegele A. mRCC Outcome in the treatment of metastatic renal cell carcinoma – a German single-center real-world experience. In Vivo. 2018 Nov-Dec;32(6):1617-22. doi: 10.21873/invivo.11422. PMID: 30348724; PMCID: PMC6365752.
18. Zanardi E, Verzoni E, Grassi P, Necchi A, Giannatempo P, Raggi D, De Braud F, Procopio G. Clinical experience with temsirolimus in the treatment of advanced renal cell carcinoma. Ther Adv Urol. 2015 Jun;7(3):152-61. doi: 10.1177/1756287215574457. PMID: 26161146; PMCID: PMC4485412.
19. Vogl UM, Zehetgruber H, Dominkus M, Hejna M, Zielinski CC, Haitel A, Schmidinger M. Prognostic factors in metastatic renal cell carcinoma: metastasectomy as independent prognostic variable. Br J Cancer. 2006 Sep 18;95(6):691-8. doi: 10.1038/sj.bjc.6603327. Epub 2006 Aug 29. PMID: 16940978; PMCID: PMC2360513.
20. Kwon WA, Cho IC, Yu A, Nam BH, Joung JY, Seo HK, Lee KH, Chung J. Validation of the MSKCC and Heng risk criteria models for predicting survival in patients with metastatic renal cell carcinoma treated with sunitinib. Ann Surg Oncol. 2013 Dec;20(13):4397-404. doi: 10.1245/s10434-013-3290-1. Epub 2013 Oct 1. PMID: 24081805.
21. Kanesvaran R, Porta C, Wong A, Powles T, Ng QS, Schmidinger M, Ye D, Malhotra H, Miura Y, Lee JL, Chong FLT, Pu YS, Yen CC, Saad M, Lee HJ, Kitamura H, Bhattacharyya GS, Curigliano G, Poon E, Choo SP, Peters S, Lim E, Yoshino T, Pentheroudakis G. Pan-Asian adapted ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of patients with renal cell carcinoma. ESMO Open. 2021 Dec;6(6):100304. doi: 10.1016/j.esmoop.2021.100304. Epub 2021 Dec 1. PMID: 34864348; PMCID: PMC8645910.
22. Motzer RJ, Jonasch E, Michaelson MD, Nandagopal L, Gore JL, George S, Alva A, Haas N, Harrison MR, Plimack ER, Sosman J, Agarwal N, Bhayani S, Choueiri TK, Costello BA, Derweesh IH, Gallagher TH, Hancock SL, Kyriakopoulos C, LaGrange C, Lam ET, Lau C, Lewis B, Manley B, McCreery B, McDonald A, Mortazavi A, Pierorazio PM, Ponsky L, Redman BG, Somer B, Wile G, Dwyer MA; CGC, Hammond LJ, Zuccarino-Catania G. NCCN Guidelines Insights: Kidney Cancer, Version 2.2020. J Natl Compr Canc Netw. 2019 Nov 1;17(11):1278-85. doi: 10.6004/jnccn.2019.0054. PMID: 31693980.
23. Escudier B, Porta C, Schmidinger M, Rioux-Leclercq N, Bex A, Khoo V, Grünwald V, Gillessen S, Horwich A; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and

follow-up†. Ann Oncol. 2019 May 1;30(5):706-20. doi: 10.1093/annonc/mdz056. PMID: 30788497.

24. Sugiyama S, Sato K, Shibasaki Y, Endo Y, Uryu T, Toyoshima Y, Oya M, Miyanaga N, Saijo N, Gemma A, Akaza H. Real-world use of temsirolimus in Japanese patients with unresectable or metastatic renal cell carcinoma: recent consideration based on the results of a post-marketing, all-case surveillance study. Jpn J Clin Oncol. 2020 Aug 4;50(8):940-7. doi: 10.1093/jjco/hyaa062. PMID: 32458996; PMCID: PMC7401718.
25. Satoh T, Koie T, Horiguchi H, Tokui N, Narita S, Ohyama C. Longer recurrence-free survival in a patient with metastatic renal cell carcinoma treated with temsirolimus. Clin Case Rep. 2017 Oct 18;5(12):1950-3. doi: 10.1002/ccr3.1181. PMID: 29225833; PMCID: PMC5715416.
26. Lee JB, Park HS, Park S, Lee HJ, Kwon KA, Choi YJ, Kim YJ, Nam CM, Cho NH, Kang B, Chung HC, Rha SY. Temsirolimus in Asian metastatic/recurrent non-clear cell renal carcinoma. Cancer Res Treat. 2019 Oct;51(4):1578-88. doi: 10.4143/crt.2018.671. Epub 2019 Apr 16. PMID: 30999721; PMCID: PMC6790860.
27. Ramaswamy A, Joshi A, Noronha V, Patil V, Sahu A, Manickam DR, Kothari R, Sable N, Agrawal A, Menon S, Prabhash K. Poor risk advanced renal cell carcinoma: outcomes from a registry in a tertiary cancer center. Indian J Med Paediatr Oncol. 2017 Jul-Sep;38(3):311-5. doi: 10.4103/ijmpo.ijmpo_154_16. PMID: 29200680; PMCID: PMC5686973.

Sažetak

USPOREDBA TERAPIJSKOG UČINKA TEMSIROLIMUSA I INTERFERONA ALFA NA PREŽIVLJAVANJE KOD BOLESNIKA S METASTATSKIM KARCINOMOM BUBREGA – KLINIČKA PRAKSA JEDNE USTANOVE

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Inhibitori faktora rasta vaskularnog endotela (VEGF) i ciljanog rapamicina (mTOR) kod sisavaca dvije su glavne skupine lijekova za ciljano liječenje metastatskog karcinoma bubrežnih stanica (mRCC). Inhibicija angiogeneze i drugih putova rasta koji su ključni za progresiju tumora dovode do značajnog poboljšanja preživljenja u bolesnika s mRCC. Glavni cilj ovog istraživanja bio je usporediti učinke temsirolimusa (mTOR inhibitor) i interferona alfa (IFN-alfa-2a) na ukupno preživljenje i preživljenje bez progresije bolesti (PFS) u bolesnika sa stadijem T3 mRCC koji su razvili metastaze u plućima u prve dvije godine nakon radikalne nefrektomije. Ukupno 60 bolesnika s dijagnosticiranim karcinomom bubrega stadija T3 koji su razvili metastaze u plućima u roku od dvije godine nakon radikalne nefrektomije uključeno je u prospektivnu studiju na Klinici za urologiju Kliničkog centra Vojvodine i djelomično retrospektivno istraživanje na Onkološkom institutu u Sremskoj Kamenici. Bolesnici su podijeljeni u dvije skupine od 30 bolesnika: liječeni temsirolimusom i liječeni IFN-alfa. Tijekom prve godine liječenja ukupno preživljenje bolesnika liječenih temsirolimusom iznosilo je 23,33%, dok je u bolesnika liječenih IFN-alfa bilo 16,67%. Prosječno preživljenje u bolesnika liječenih temsirolimusom bio je 9,3 mjeseca, dok je u bolesnika liječenih IFN-alfa iznosilo 6,9 mjeseci i ta razlika je bila statistički značajna (p=0,028). Bolesnici liječeni temsirolimusom pokazali su statistički značajno duži medijan PFS u usporedbi s bolesnicima liječenim IFN-alfa (p<0,0085). U zaključku, terapija temsirolimusom ima značajno pozitivan učinak na preživljenje bolesnika s mRCC. Bolesnici liječeni temsirolimusom pokazuju značajno duže prosječno preživljenje i prosječan PFS u usporedbi s bolesnicima liječenim IFN-alfa.

Ključne riječi: *Karcinom bubrežnih stanica; Temsirolimus; Interferon alfa; Preživljavanje*