TO CASTRATION RESISTANT PROSTATE CANCER TREATMENT MODERN APPROACHES

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Annotatsion. From 60 years old increased at least every hundredth male this disease with gets sick. From 70 years old then every eighth male this to illness exposed Metastatic to hormones resistant prostate cancer in treatment chemotherapy both in monoregime and in other drugs with together application todays on the day standard is considered. Many in cases prostate cancer hormonal androgen deprivation therapy (therapeutic castration) is good answer Unfortunately, time to pass with many in patients treatment continue to the extent despite, tumor develop Testosterone begins. decrease in malignant cells growth stop for enough This situation will not happen. to the hormone resistant to hormone resistant or to castration resistant prostate It is called cancer. Treatment the results improve for medicines, their combinations and prostate with breast cancer sick patients for new therapy modes search continue is doing.

Key words: prostate diaper cancer, chemotherapy, fire resistant, average safe stay

СОВРЕМЕННЫЕ ПОДХОДЫ К ЛЕЧЕНИЮ КАСТРАЦИОННО-РЕЗИСТЕНТНОГО РАКА ПРЕДСТАТЕЛЬНОЙ ЖЕЛЕЗЫ

Аннотация. С 60 лет увеличилось как минимум каждое сотое мужское лицо, страдающее этим заболеванием. С тех пор, начиная с 70 лет, каждый восьмой мужчина подвергался этому заболеванию. Метастатический гормонорезистентный рак предстательной железы в лечении химиотерапии, как в монорежиме, так и в других препаратах с совместным применением, сегодня считается стандартным. Во многих случаях рак предстательной железы гормональная андрогенодефицитная терапия (терапевтическая кастрация) является хорошим ответом. К сожалению, время, чтобы пройти со многими пациентами, продолжается в той мере, в какой, несмотря на развитие опухоли, тестостерон начинается. уменьшение злокачественных клеток рост останавливается достаточно. Эта ситуация не произойдет. к гормону устойчивому к гормону устойчивому или к кастрации устойчивому простате Он называется раком. Результаты лечения улучшаются для лекарственных

препаратов, их комбинаций и пациентов с раком предстательной железы с раком молочной железы, продолжается поиск новых режимов терапии.

Ключевые слова: рак подгузников простаты, химиотерапия, огнестойкость, безопасное среднее пребывание

Relevance. Prostate diaper cancer in treatment right approaches the patient's life quality extension and to improve opportunity However, this in the direction active to research despite, many clinical research still big to achievements did not reach and treatment the results noticeable at the level did not improve. Tah 327 and SWOG 9916 [1, 2] study results announcement since done then with Taxotere (docetaxel). chemotherapy (CT) metastatic to hormones resistant (GH) prostate 1 — line for cancer (RPH)-GRPJ and treatment is the standard. Many researchers to hormones endurance heterogeneous disease they admit that and todays on the day standard there is although, this pathology treatment according to many questions there is are, they are at symposia literature and in discussions " what? When? to whom? ». CT docetaxel with metastatic GRPJ, rule as a rule, diagnosis from being placed then done Metastatic not been of nature hormone resistance (biochemical development) has been identified in case, above counting passed questions appearance Docetaxel with treatment in the background in patients biochemical or clinical development development with further complicated situation to the surface comes. Question is born: then what to do Need it? Second row still not determined. The patient symptomatic for treatment transfer is it necessary or to him/her to oneself typical medicine therapy continue to hold opportunity Is there any? Checked problems this in the article discussion is being done. The current to the day until wide Treatment of disseminated RPJ palliative become remains. With metastatic BPH sick in 70-80 % of patient’s androgens lack within 18-24 months symptomatic to improve and prostate to oneself typical antigen (PSA) level to decrease take will come, but later in patients’ hormonal resistance develops. Hormone use of 2nd line chemotherapy (HT) attempts of patients only one in part short term into remission to achieve help gives. Next development 12 months average safe stay with to death take comes [1, 2]. The current at the time wide with dispersed GFRP sick of patient’s various populations for approaches determination need. Home Questions: with metastatic GRPZ sick When CTNI in patients start Need it? Asymptomatic wide with diffuse RPH sick patients’ docetaxel with treatment Is it necessary? Today to the day until in literature this to questions reliable answer no. " For " and " against" arguments There is a disease. initial Using CT in stages still safe stay level to increase help does not give, but this toxicity to develop and previous medicine resistance to the beginning take arrival possible. Apparently as it stands, the effective 2nd line appearance from being before, docetaxel individual course of the disease into account received without usage need. Tah 327 research analysis publication from being before, experts’ opinion based on

one row recommendations PSA level was given. two even increase time slowly was asymptomatic in patients' mandatory observation offer was done. Only in the bones symptomatic metastases was and PSA value slowly two even increase was to patients second grade HT ketoconazole Zometa and palliative radiation with therapy (lt) together transfer recommendation PSA level was fast growth and high two even increase, symptoms and / or visceral metastases existence with sick to patients to docetaxel CT based on PSA was shown. clinical forms symptoms and metastases existence or to the absence looking at This relationship is different. with patients into 4 categories to be possible [3]: 1) PSA level growth – only biochemical development; 2) asymptomatic metastases – limited lesion; 3) asymptomatic metastases – extensive widespread; 4) symptomatic metastases. Table with GRPJ sick of patients various CT scan in groups indicators shown, this GRPJ is heterogeneous disease that again one there is confirms. Current to the day until asymptomatic patients' treatment from where starts need about question open remains. Transferring the 2nd line of Gt is it necessary or start CTNI better, debatable become This is issue confirmation and solution to do for additional clinical research transfer need. Another one important Question: What is CT in men? minimal manifestation of symptoms to be with start or from metastases clinical of appearance further brighter manifestation to be wait. That's it. into account to take docetaxel with treatment in the process of symptoms clinical Decreased PSA to decrease than less occurs [1]. Painless patients pain syndrome to those who have than 10 CT cycles better tolerance they do. This attitude with, if symptoms developing and / or growing going if, also, close in the future negative clinical appearance's development danger high if, then KT appointment recommendation Such PSA level in certain situations two even increase on time justification need. Tah 327 research results this showed that asymptomatic in patients From Taxotere when using average safe stay 21.3 months, various symptoms was in patients and 14.2 months organization [4]. From this except, Htni docetaxel with early application life of quality to deteriorate take arrival possible in mind catch In the Tach 327 study, in general life, in short quality from taxonomy when using compared to mitoxantrone [1] much good was although minimally symptomatic of patients small in the group, especially docetaxel weekly introduction with, life of quality deterioration record [5]. This important point, as well as treatment plan in the making patients with discussion to be done and discussion to be done This is necessary. in stages time about clear answer no, i.e. when and how CT docetaxel in cases with start need. Retrospective multivariate analysis held and Taxidermy with 1, 2 and 5 years of treatment safe stay forecast assessment for used to the clinic, PSA level to the dynamics and independent prognostic to factors based models was created [6]. Clinical characters are also taken into account taken from : research started in the period of pain the presence of PSA elementary level, age, beginner to the state relatively development type (bones) while scanning measured formations or new of

the hearths appearance to be), in the liver metastases existence and metastatic of the hearths number. AJ Armstrong et al. [6] PSA level dynamics retrospective analysis conducted, in which PSA elementary value < 114 ng/ml and his/her two even increase 55 days was in patients safe stay level noticeable at the level improved. S. Oudard and others by take visited In the study [7, 8], PSA levels kinetics and with GRPF sick in patients pain syndrome importance confirmed. PSA value > 45 days inside two even increased and pain syndrome not been of patients average safe stay level 32.4 months organization PSA level two even increase time < 45 days was and strong pains was patients in the group average safe stay level only 8 months organization reached. PSA level kinetics importance other It has also been confirmed in studies [9, 10] that important prognostic factor as. Therefore for, with GRRPZ sick patients treatment in tactics necessary condition PSA level kinetics is to detect, especially for CT with DOCETAXEL clear instructions if not, this including asymptomatic in patients or PSA indicator only according to development record done in patients. PSA content kinetics assessment to the patient and his/her to relatives of the disease forecast and using CT possible was positive impact about information to give help gives. From this except for the disease to go prophecy to do many inconvenient factors and PSA level two even increase very short time if, docetaxel use life see duration a little to increase help gives, as well as his/her to the quality impact does. So so, CT Taxotere-this is with GRPJ sick patients The only way to treat it. However, the treatment start time issue still controversial.PSA level slowly development with in the case of GRPF without metastasis gt Using line 2 of possible. Patients this in the category docetaxel appointment about PSA 's decision initial indicator and his/her two even increase time into account received individually acceptance will be done.

Material and methods. Metastatic PPH and bone development was patients every 3 weeks one times Taxotere therapy they receive need. Taxidermy with repetitive treatment current to the day until, if they docetaxel with treatment if they stop, with GRPF sick patients next treatment study according to intensive research take is going on. Some patients of the disease development, clearly toxicity development (III–IV degree) or to therapy maximum at the level positive answer to take because of treatment If the treatment since the beginning positive impact If it shows, Taxidermy with treatment duration todays on the day not determined. Docetaxel then development in the case of only mitoxantrone drug as confirmed, its purpose palliative impact to show Docetaxel is possible. from therapy after when used in the 2nd line, 24 (3-37) months not achieved, average safe stay level 15.3 (3-32) organization Docetaxel does. again, acceptance from doing then appearance was main side effects leukopenia, alopecia and fatigue was. Of the patients no one therapy from the deadline before not stopped. With metastatic GRPJ sick in patients' docetaxel in the 2nd and 3rd lines of therapy use about messages available. J. Ansari et al. [17] docetaxel + prednisolone 1st line of treatment with an interval of 3 weeks 107 patients

treated about information presented PSA 's average elementary The value is 185 (6.62000) ng/ml. organization this.this 22 people from the group to the patient later the 2nd, 7th and 3rd HT lines docetaxel with was held. Held in rows 1, 2 and 3 cycles number suitable 650, 119 and 38 respectively organization The whole in the cohort in 59 percent of patients docetaxel with primary to therapy answer given. Positive results (PSA level) decrease >50 %) suitable accordingly after the 2nd and 3rd application of the drug primary answer gave in 90 and 71 percent of patients obtained. In rows 1, 2 and 3, III-IV-degree neutropenia development recorded at 2.9 made; suitable 4.2 and 5.2% of cases, respectively. On average safe stay 15.9 months organization the above research information response to 1st line of therapy received in patients Taxotere again use opportunity showed. Docetaxel primary resistance and next treatment choice problem become remains, because the 2nd CT line determination search New cytostatics and targeted drugs with combinations is being studied. R. Epplen et al. [18] reported that docetaxel was administered in the first line from what he did then PSA level 2nd line therapy in 23 advanced GFRP patients' docetaxel and bevacizumab combination application efficiency having studied After the 1st line of therapy disease-free of the era median 6.2 (311) months equal was. Line 2 begins PSA content up to two even increase 5.9 (28) months organization Docetaxel acceptance to do every week 35 mg/m 2, bevacizumab – 10 mg/kg in 2 weeks one times prescribed. 2nd line of treatment from the beginning PSA level before average 189.4 (951200) ng/ ml 16 (69.5%) patients had PSA levels greater than 50%. to regression has. Average 29 months old observation during average safe stay 17.5 (3-32) months organization Bevacizumab introduction because of hypertension development in 21.7% of cases record the drug was acceptance to do as a result clear proteinuria appearance to be because of one patient from research was released. Authors stated that patients with GRPP develop docetaxel and bevacizumab combination use satisfactory at the level accounting will be done and docetaxel with after 1st line of treatment record PSA level fast two even increase for choice method become service to do A. Heidenreich et al. [19] used the combination of docetaxel + bevacizumab docetaxel again send with compared to application according to information presented 59 patients docetaxel from therapy then development Patients were observed. to groups divided: docetaxel on day 1 for 3 weeks during 35 mg/m2 per week, 4 weeks off; 2 weeks off - docetaxel 25 mg/m2 at weekly intervals and bevacizumab- 10 mg/kg every 2 weeks. Those who received 1st line of therapy all patients with PSA\u003e 30% decrease record in general when taking, after the 2nd row is passed then, in 40 out of 59 cases (67.8%) the whole >30% decrease in PSA in the group record in group 1, there were no patients with the disease. safe stay 6.2 months, overall, 13.3 months, 8.9 and 17.5 months in group 2. Bevacizumab hypertension in the form of send with related toxicity in 17.8 % of patients observed in 1 patient high level proteinuria development because of treatment discontinued. In the 1st line of therapy in the Swog

9916 protocol docetaxel + estracit from the combination use studied. O. Caffo [20] et al. docetaxel against the background of 1st line therapy happened was from development then this from the combination use efficiency about information presented Docetaxel was administered. administration on day 2 from day 1 to day 5 of the cycle for 3 doses 840 mg daily, divided in dose estracite mouth through application with together done increased. PSA level regression in 52% of cases record Progression - free average safe stay level 15, general safe stay level 61 weeks. So, in monotherapy Taxotere again including Taxotere in the 2nd line of treatment other drugs with from the combination use with progressive GRPJ sick in patients effective This will be complicated clinical in the situation still standard approach there is not. However, in research taken information optimism strengthens and this complicated in the category patient's treatment the results further to improve hope does. Current at the time docetaxel after using then effective in line 2 was medicines find according to research active take O. Sartor and et al. [21] cabazitaxel prednisolone with combination previously with CT treated in patients' application III stage on research the results presented reached, its main drug Taxotere (Tropic Trial) was. Cabazitaxel, also a half- synthetic taxon to the group enters and his/her chemical in the formula docetaxel to the formula relatively two radical changes available. Impact mechanism from oncourology 1 ' 201 clinic previous in research of the drug to docetaxel resistant tumor to the models relatively efficiency proven. This The study was conducted in 146 centers in 26 countries, including including In Russia conducted. A total of 755 patients included. Stratification of patient's activity status (ECOG scale 0, 1) and 2 vs. measurable and immeasurable formations according to dun Patients were divided into 2 groups. randomized: in 1 they were given 25 mg/m2 at a dose of 25 mg/m2 prednisolone with together 10 mg/ day, mitoxantrone 12 mg/m2 on day 2 prednisolone with together one at different intervals sent. The research main purpose general safe to stay assessment was, secondary disease-free safe stay, regression frequency and tolerance analysis to do the study was conducted using RECIST criteria. according to measurable progressive to diseases played patients own inside bought, new furnaces or PSA level according to development.

Conclusion. The patients were matched for disease severity, demographics, and other characteristics. The median overall survival in the mitoxantrone group was 12.7 months compared with 15.1 months in the cabazitaxel group (hazard ratio 0.72, 95% CI 0.61–0.84). The differences were significant ($p < 0.0001$). The median progression-free survival was 2-fold higher in the cabazitaxel group than in the mitoxantrone group, at 2.8 months and 1.4 months, respectively ($p = 0.0002$). PSA and time to progression were also better in the cabazitaxel group. In the toxicity and tolerability study, the most common grade III–IV adverse events in the CABAZITAXEL group were febrile neutropenia (7.5% of cases) and diarrhea (6.2%). Thus, in this study, the use of cabazitaxel was associated with improved overall

survival (compared to the results obtained with mitoxantrone), a 28% reduction in the risk of death, as well as an increase in the median time to PSA progression and response. The findings suggest that cabazitaxel is a potential new drug that can be used to treat patients with GRP after docetaxel therapy. Cabazitaxel is currently included in the recommendations of the European Association of Urology as a 2nd-line drug for patients who have progressed after 1st-line docetaxel therapy [22]. Cabazitaxel is currently only registered in the United States. In conclusion, it should be noted that the treatment of patients with GRPJ remains a difficult problem. A differentiated approach to the treatment of these patients, taking into account their clinical condition, PSA level kinetics and other indicators, allows for the right decision. Taxotere use in the 1st line of therapy the most effective treatment method of patient's life quality extension and to improve help gives. A series in patients Taxotere again to enter, as well as the drug application with related of quality noticeable at the level without deterioration his life to extend opportunity gives. To Taxotere based new 1st-line therapy schemes working exit active search topic to be treated the results later improve for the purpose done increased. Cabazitaxel used without take visited research, its treatment the results improve for new opportunities created, docetaxel from therapy after developed with progressive GRPJ sick in patients him a level 2 prospect medicine as application efficiency showed. Hormone therapy with CRP sick patients' treatment for standard is considered, but stabilization from the era then many in patients' disease to develop and castrate resistant to form has will be. Patients this group management tactics modern clinical oncology complicated is a problem. Wide in a disseminated malignant process surgery and radiation from therapy use opportunities very limited, therefore for treatment leader method to docetaxel based primary chemotherapy. Unfortunately, this from the method use the possibilities are also limited, because after 6-8 months then all in patients of the disease recurrence develops. Many clinical research results this shows that different kind impact to the mechanisms has drugs from the combination use therapeutic the effect strengthens.

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