Паллиативная лучевая терапия рака легкого

Динамика показателей заболеваемости и смертности от ЗНО легких (С33-34) населения Челябинской области и РФ за период 2006-2015 гг. (грубый показатель)

Данные представлены сотрудниками Оргметодотдела Аксеновой И.А Доможировой А.С Новиковой Т.С из доклада «Анализ выживаемости пациентов с ЗНО легких в Челябинской области»

Динамика стадийной структуры ЗНО легких (С33-34) в Челябинской области за период 2006-2015 гг.

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National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2018
Non-Small Cell Lung Cancer

Advanced Stage/Palliative RT

- **The dose and fractionation of palliative RT should be individualized based on goals of care, symptoms, performance status, and logistical considerations. Shorter courses of RT provide similar pain relief as longer courses, but with a higher potential need for retreatment,[86-89] and are preferred for patients with poor performance status and/or shorter life expectancy. For palliation of thoracic symptoms, higher dose/longer-course thoracic RT (eg, ≥30 Gy in 10 fractions) is associated with modestly improved survival and symptoms, particularly in patients with good performance status.[90,91] When higher doses (>30 Gy) are warranted, technologies to reduce normal tissue irradiation (at least 3D-CRT and including IMRT or proton therapy as appropriate) may be used.**

Palliative RT			
• Obstructive disease (SVC syndrome or obstructive pneumonia)	30–45 Gy	3 Gy	2–3 weeks
• Bone metastases with soft tissue mass	20–30 Gy	4–3 Gy	1–2 weeks
• Bone metastases without soft tissue mass	8–30 Gy	8–3 Gy	1 day–2 weeks
• Brain metastases	CNS GLs*	CNS GLs*	CNS GLs*
• Symptomatic chest disease in patients with poor PS	17 Gy	8.5 Gy	1–2 weeks
• Any metastasis in patients with poor PS	8–20 Gy	8–4 Gy	1 day–1 week

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NCCN Guidelines Version 2.2018
Small Cell Lung Cancer

Extensive Stage:

- Consolidative thoracic RT is beneficial for selected patients with extensive-stage SCLC with CR or good response to systemic therapy. Studies have demonstrated that consolidative thoracic RT up to definitive doses is well tolerated, results in fewer symptomatic chest recurrences, and improves long-term survival in some patients.[21,22] The Dutch CREST randomized trial of modest-dose thoracic RT (30 Gy in 10 fractions) in patients with extensive stage SCLC that responded to systemic therapy demonstrated significantly improved 2-year overall survival and 6-month PFS, although the protocol-defined primary endpoint of 1-year overall survival was not significantly improved.[23] Subsequent exploratory analysis found the benefit of consolidative thoracic RT is limited to the majority of patients who had residual thoracic disease after systemic therapy.[24]
- Dosing and fractionation of consolidative thoracic RT should be individualized within the range of 30 Gy in 10 daily fractions to 60 Gy in 30 daily fractions, or equivalent regimens in this range.

Показания к проведению паллиативного курса

- Рак легкого III стадии при наличии противопоказаний к радикальной лучевой терапии (общий статус ECOG 3-4) для устранения или предупреждения симптомов заболевания (ССВПВ; боль в грудной клетке; обструкция крупных бронхов, включая обструктивную пневмонию; кровохарканье, одышка, кашель).
- НМРЛ IV ст при общем статусе ECOG 0-2 и при наличии симптомов заболевания или риска их развития (ССВПВ, боль в грудной клетке; обструкция крупных бронхов, включая обструктивную пневмонию; кровохарканье, одышка, кашель).

Table 1. Symptom palliation in major prospective randomized clinical trials on palliative thoracic radiotherapy for non-small-cell lung cancer.

Study (year)	Patients included (n)	Response rate (%)				Ref.
		Hemoptysis	*Cough*	*Chest pain*	*Dyspnea*	
MRC (1991)	369	81–86	56–65	75–80	57–66	[8]
MRC (1992)	233	72–75	48–56	59–72	41–43	[9]
MRC (1996)	509	89–95	36–48	50–58	37–46	[10]
Nestle *et al.* (2000)	152	80–82	69–80	74–76	NR	[21]
Sundstrom *et al.* (2004)	421	80–90	20	NR	40	[22]
Erridge *et al.* (2005)	149	87–97	51–58	84	NR	[23]
Senkus-Konefka *et al.* (2005)	100	86	51	83	60	[7]

Cancer Science
Japanese Cancer Association JCA
Open Access

Meta-analysis comparing higher and lower dose radiotherapy for palliation in locally advanced lung cancer

Jie-Tao Ma,[1] Jia-He Zheng,[2] Cheng-Bo Han[1] and Qi-Yong Guo[2]

The purpose of this meta-analysis was to compare higher dose (≥30 Gy) and lower dose (<30 Gy) radiotherapy (RT) on palliation of symptoms and survival in patients with locally advanced lung cancer.
The primary outcome was palliation of symptoms (cough, chest pain, hemoptysis), and 1- and 2-year overall survival. Five randomized controlled trials with a total of 1730 patients with lung cancer were included in the meta-analysis. There were 925 patients treated with a higher RT dose (≥30 Gy) and 805 treated with a lower RT dose.
In conclusion:both dosages provided equal symptom relief, and 1- and 2-year OS were similar with the two dosages

First author	Year	RT regimen							
		Higher dose group (≥30 Gy)				Lower dose group (<30 Gy)			
		Gy	Number of fractions	Duration (weeks)	BED (Gy_{10})	Gy	Number of fractions	Duration (days)	BED (Gy_{10})
Kramer([13])	2005	30	10	2	33.5	16	2	8	28.0
Erridge([14])	2005	30	10	2	33.5	10	1	1	24.8
Sundstrøm([15])	2004	42	15	3	42.7	17	2	8	30.7
		50	25	5	37.8				
Macbeth([16])	1996	39	13	2.5	42.4	17	2	8	30.7
Medical Research Council([17])	1991	30	10	2	33.5	17	2	8	30.7

BED was calculated based on the formula of Fairchild *et al.*([10]): BED (Gy10) = $n\,d\,[1 + d/(\alpha/\beta)] - \mathrm{Ln}\,2\,(T - T_{ko})/(A)\,(T_p)$, where: α/β ratio = 10; T, overall treatment time; T_{ko} (kickoff time for accelerated repopulation) = 7; A = 0.35 (as a measure of intrinsic radiosensitivity); T_p (effective doubling time) = 2.5 days; d, dose per fraction; n, number of fractions; RT, radiotherapy.

Palliative Thoracic Radiotherapy for Lung Cancer: A Systematic Review

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Methods

RCTs comparing two or more dose fractionation schedules were reviewed using the random-effects model of a freely available information management system. The relative risk and 95% CI for each outcome were presented in Forrest plots. Exploratory analysis comparing dose schedules after conversion to the time-adjusted biologically equivalent dose (BED) was performed to investigate for a dose-response relationship.

Results

A total of 13 RCTs involving 3,473 randomly assigned patients were identified. Outcomes included symptom palliation, overall survival, toxicity, and reirradiation rate. For symptom control in assessable patients, lower-dose (LD) RT was comparable with higher-dose (HD), except for the total symptom score (TSS): 65.4% of LD and 77.1% of HD patients had improved TSS ($P = .003$). Greater likelihood of symptom improvement was seen with schedules of 35 Gy_{10} versus lower BED. At 1 year after HD and LD RT, 26.5% versus 21.7% of patients were alive, respectively ($P = .002$). Sensitivity analysis suggests this survival improvement was seen with 35 Gy_{10} BED schedules compared with LDs. Physician-assessed dysphagia was significantly greater in the HD arm (20.5% *v* 14.9%; $P = .01$), and the likelihood of reirradiation was 1.2-fold higher after LD RT.

Table 2. Randomized studies comparing different doses and fractionation schedules in palliative thoracic radiotherapy for lung cancer.

Study (year)	Patients included (evaluated) (n)	Radiation schedules compared	Effect of intervention in terms of survival	Effect of intervention in terms of palliation	Ref.
Simpson *et al.* (1985)	409 (316)	40 Gy in 8 fractions (split course) in 4 weeks 40 Gy in 20 fractions in 4 weeks 30 Gy in 10 fractions in 2 weeks	6.2 months† 6.9 months† 6.4 months†	Approximately 60% of symptom decrease without difference for treatment arm	[27]
Teo *et al.* (1988)	291 (273 for symptoms assessment)	45 Gy in 18 fractions and 4.5 weeks 31.2 Gy in 4 fractions and 4 weeks	20 weeks† 20 weeks†	71%‡ 54%‡ $p < 0.02$	[28]
MRC (1991)	369	30 Gy in 10 fractions and 2 weeks 17 Gy in 2 fractions and 8 days	177 days† 179 days†	86, 56 and 75%§ 81, 65 and 80%§ p = NS	[8]
MRC (1992)	235 (233)	17 Gy in 2 fractions and 8 days 10 Gy in a single fraction	100 days† 122 days† p = NS	75, 48 and 59%§ 72, 56 and 72%§ p = NS	[9]
Abratt *et al.* (1995)	84	35 Gy in 10 fractions and 2 weeks 45 Gy in 15 fractions and 3 weeks	8.5 months† 8.5 months†	68%‡ 76%‡ p = NS	[29]
MRC (1996)	509	39 Gy in 13 fractions and 2.5 weeks 17 Gy in 2 fractions	1. 9 months† 2. 7 months† p = 0.03	89, 36 and 50%§ 95, 48 and 58%§ p = NS	[10]
Rees *et al.* (1997)	216	22.5 Gy in 5 fractions and 5 days 17 Gy in 2 fractions and 1 week	23%¶ 18%¶ p = NS	No difference; exact numbers not provided	[30]
Nestle *et al.* (2000)	152	60 Gy in 30 fractions and 6 weeks 32 Gy in 16 fractions twice daily, in 10 days	36%¶ 38%¶ p = NS	80, 69 and 74%§ 82, 70 and 76%§ p = NS	[21]
Bezjak *et al.* (2002)	230	20 Gy in 5 fractions and 5 days 10 Gy in a single fraction	6 months† 4.2 months† p = 0.03	Change of LCSS: 10.1 points Change of LCSS: 1.46 points p = 0.009	[5]
Sundstrom *et al.* (2004)	421	50 Gy in 25 fractions and 5 weeks 42 Gy in 15 fractions and 3 weeks 17 Gy in 2 fractions and 8 days	6.8 months† 7.0 months† 8.2 months† p = NS	No difference in numerous assessments	[22]

Исследование где бы не проводилась ЛТ вообще и проводилась паллиативная?

Цель исследования

Задачи

- Оценить общую выживаемость в группе больных раком легкого, получивших паллиативный курс ДЛТ в рамках РООП за период с 2010 по 2017 г
- Провести подгрупповой анализ общей выживаемости в зависимости от возраста, стадии, морфологии опухоли, общего статуса больного.
- Попытаться стратифицировать пациентов в зависимости от полученных данных на группы, для каждой из групп определить показания для проведения «низкодозной» лучевой терапии (гипофракционирование) и «высокодозной» (более 30 изоГр в традиционном, либо динамическом режиме) ЛТ.

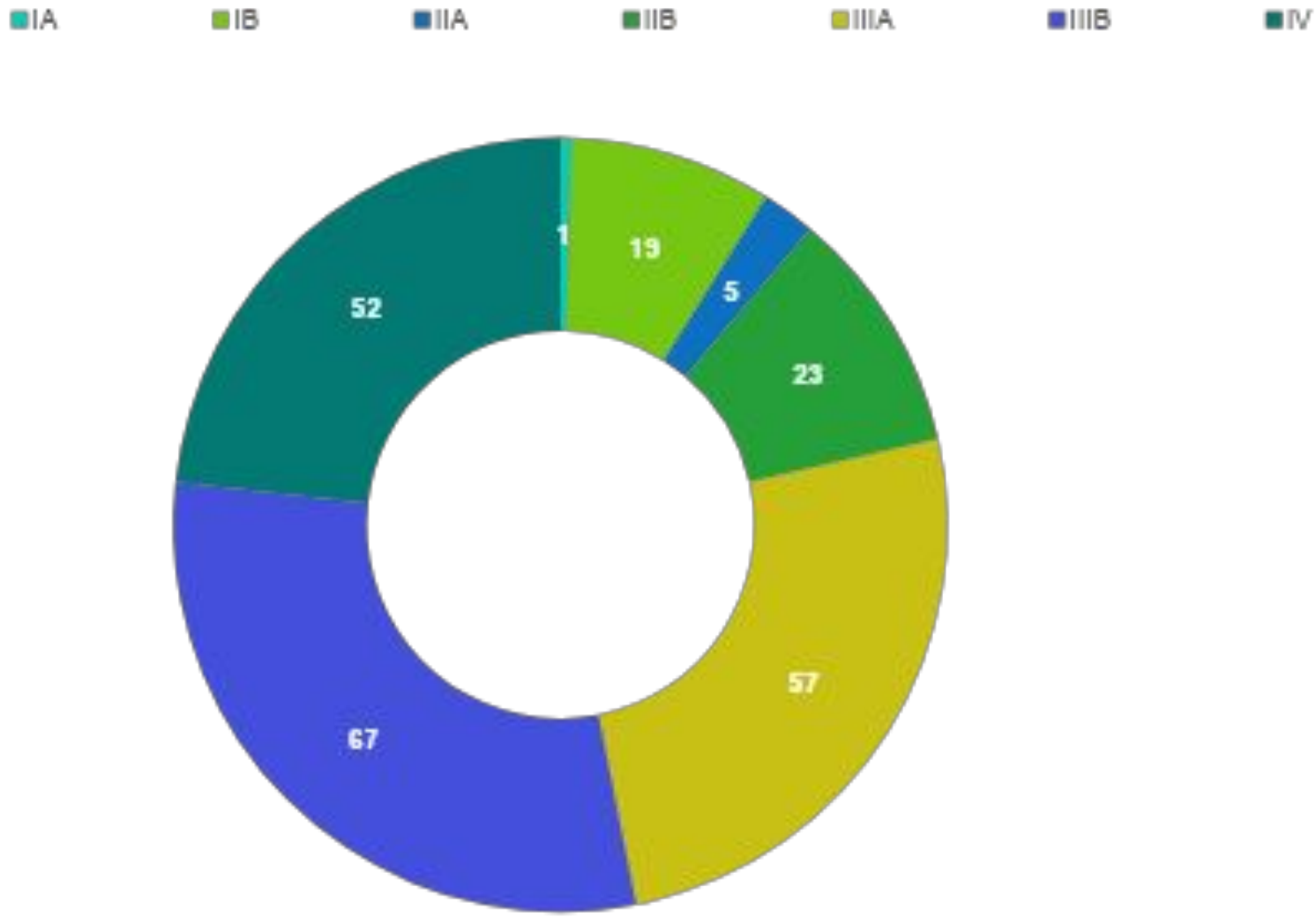
Материалы и методы

- В период с 2010 по 2017 г паллиативный курс в РООП ЧОКЦО и ЯМ получили 224 человека
- Средний возраст составил 71,4
- Женщины 53 (22,3%)
- Мужчины 171 (77,7%)
- Все пациенты были пролечены методом ДЛТ на аппарате Theratron Equinox с использованием 2D планирования

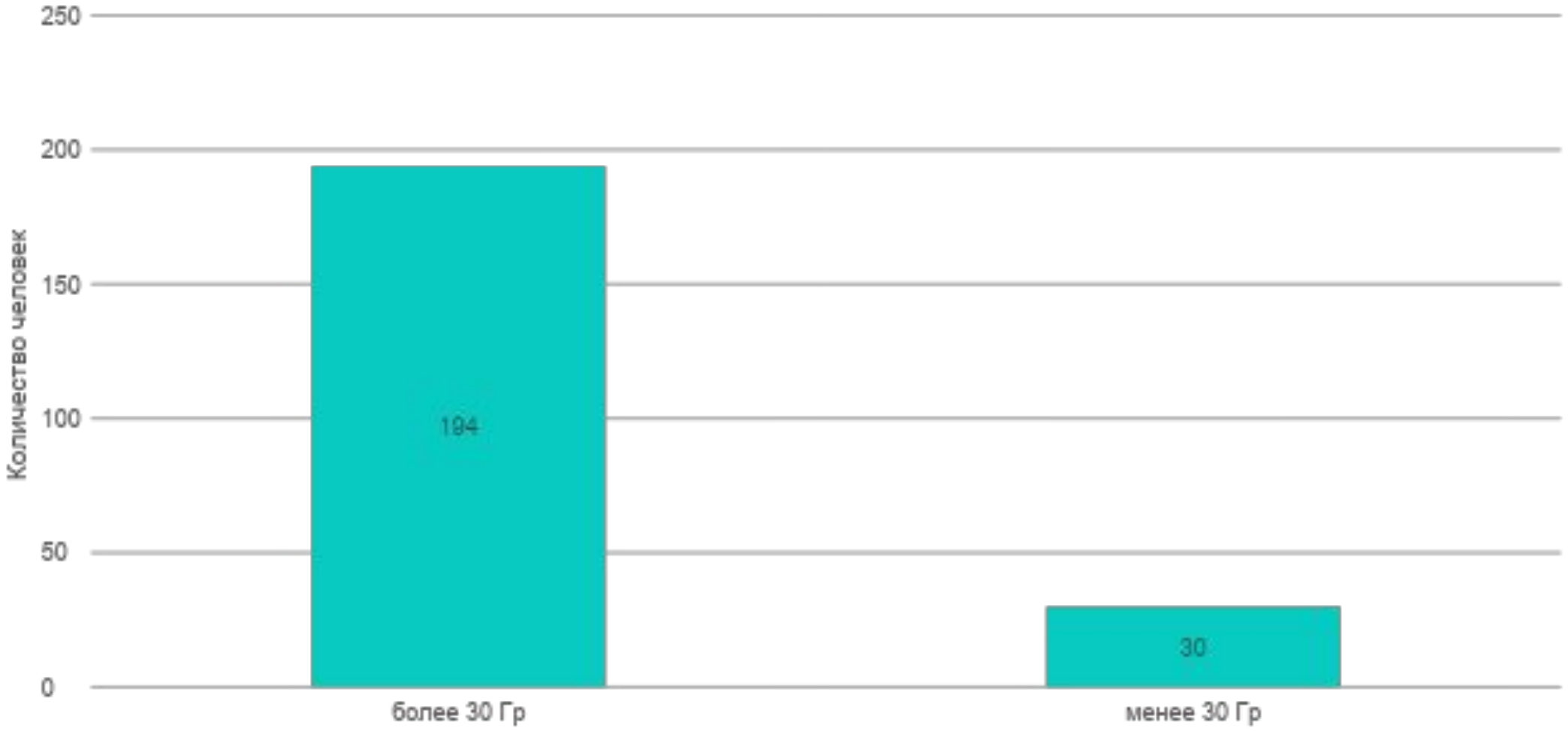
Критерии исключения

- Получавшие одновременно с ЛТ ПХТ
- Пациенты, подвергшиеся повторному облучению
- Пациенты, пролеченные иным способом (с помощью брахитерапии)
- Пациенты пролеченные иным способом (3D CRT ,IMRT , SBRT и проч)

Распределение по стадиям

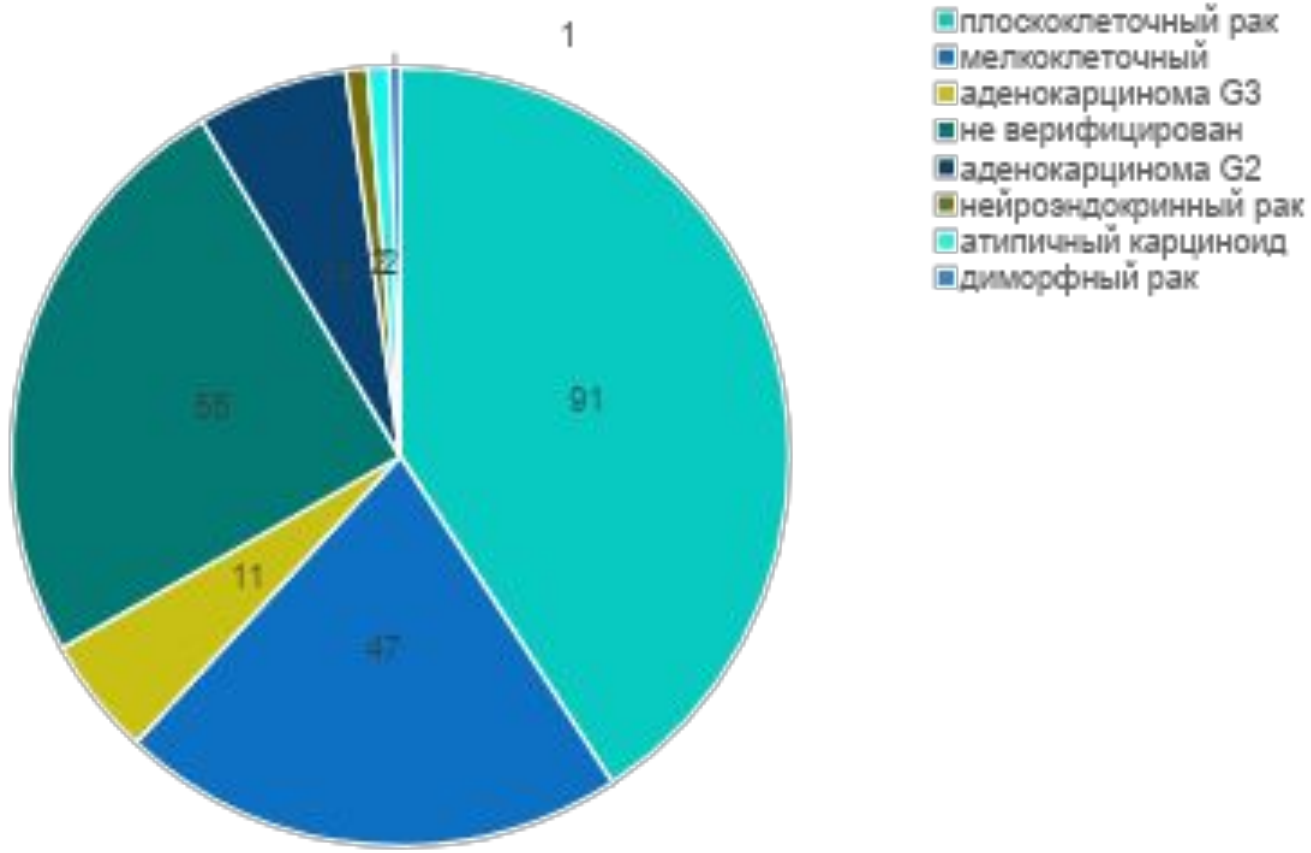


Распределение по подведенной дозе

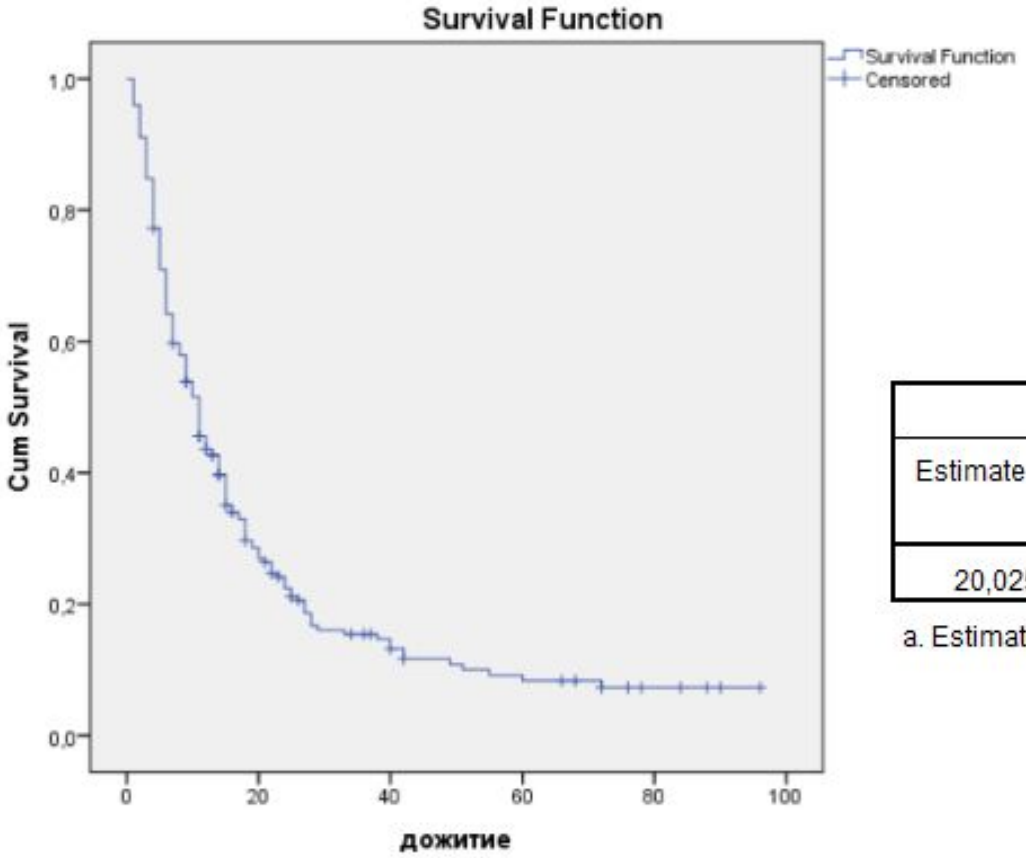


82% 18%

Распределение по гистологической структуре



Общая выживаемость

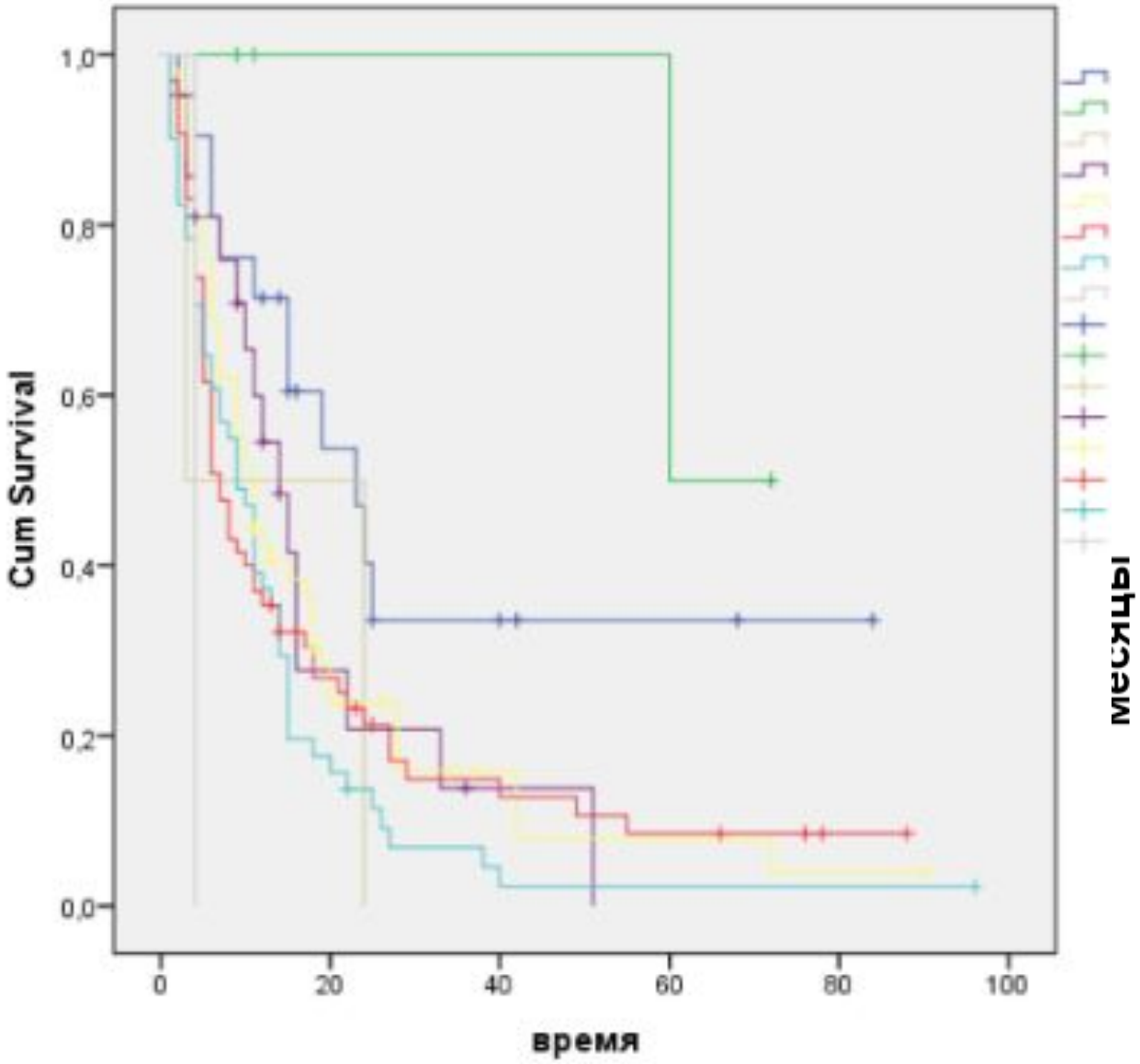


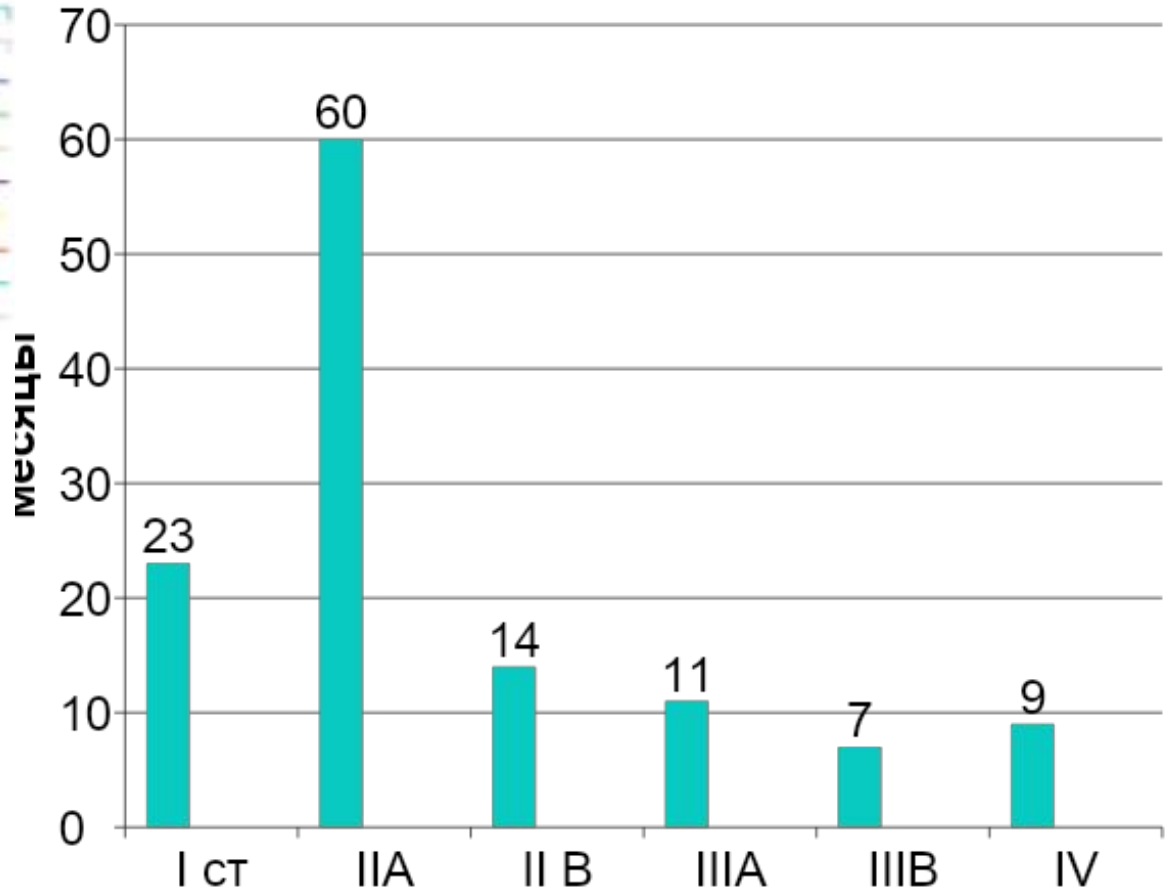
Means and Medians for Survival Time

Mean[a]				Median			
Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound			Lower Bound	Upper Bound
20,025	1,869	16,362	23,689	11,000	,940	9,158	12,842

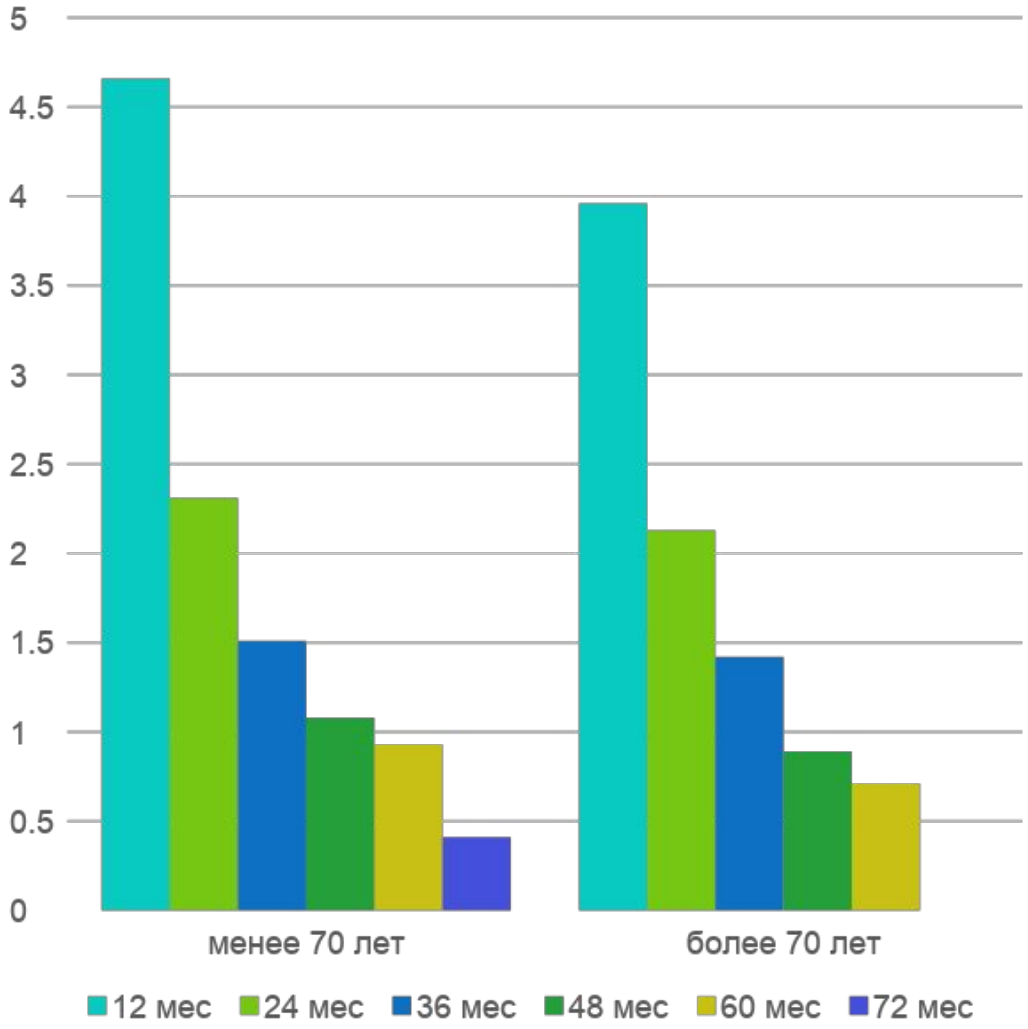
a. Estimation is limited to the largest survival time if it is censored.

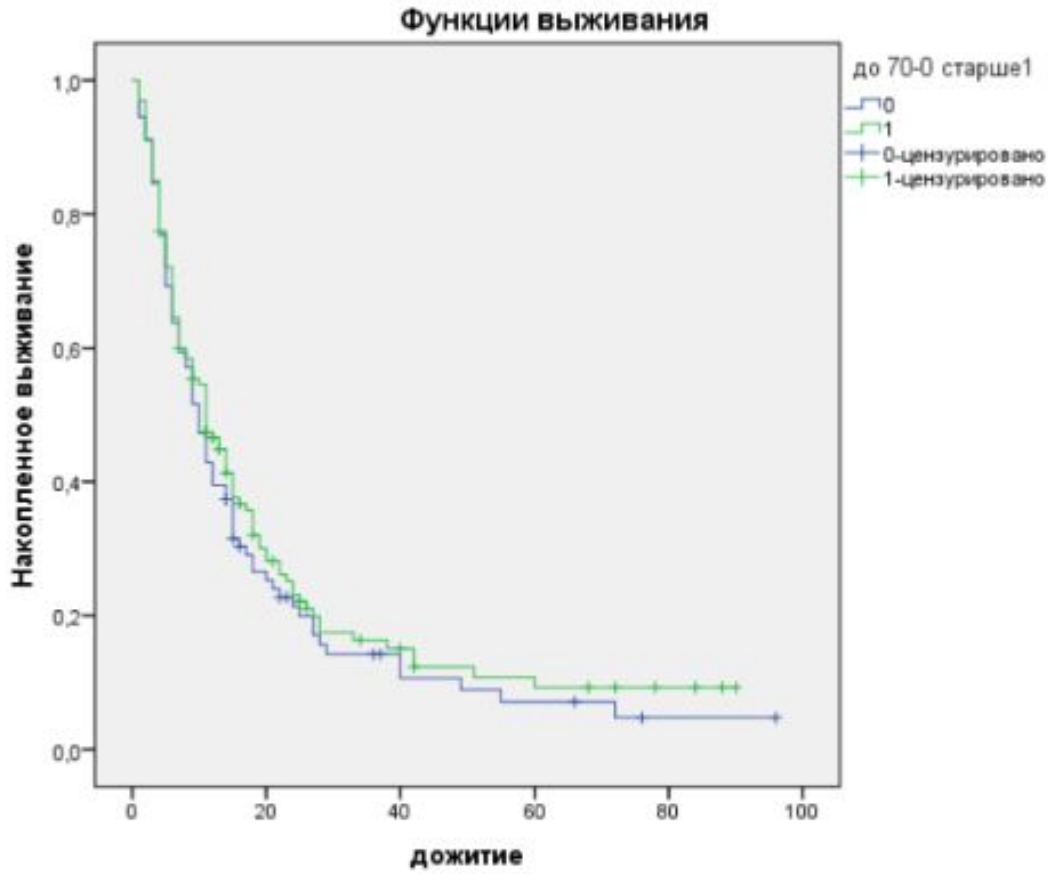
ОВ в зависимости от стадии





ОВ в зависимости от возраста



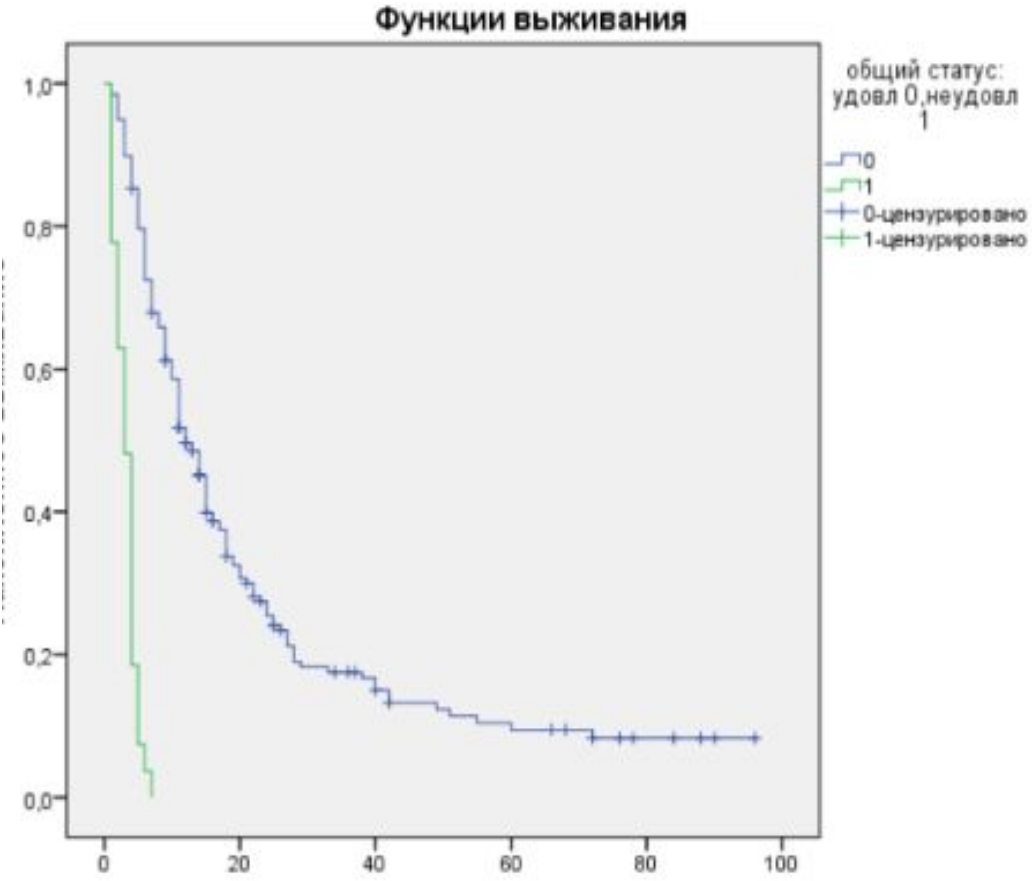


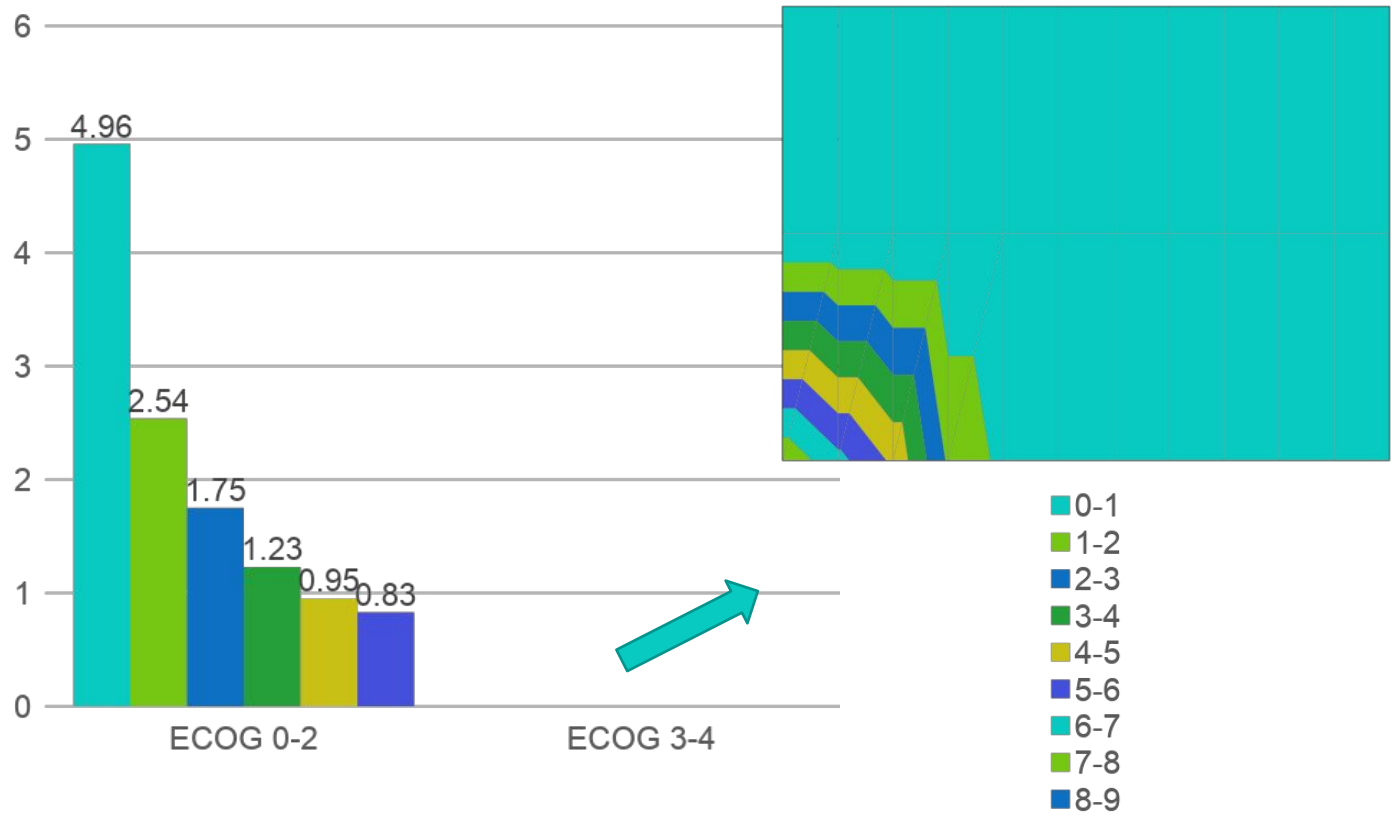
P >0,05

Средние значения и медианы для времени выживания

до 70-0 старше1	Среднее значение[a]				Ме	
	Оценка	Стандартная Ошибка	95% доверительный интервал		Оценка	Стандартная Ошибка
			Нижняя граница	Верхняя граница		
0	18,273	2,580	13,217	23,329	10,000	1,099
1	20,765	2,459	15,945	25,585	11,000	1,671
Все	20,025	1,869	16,362	23,689	11,000	,940

ОВ в зависимости от общего статуса



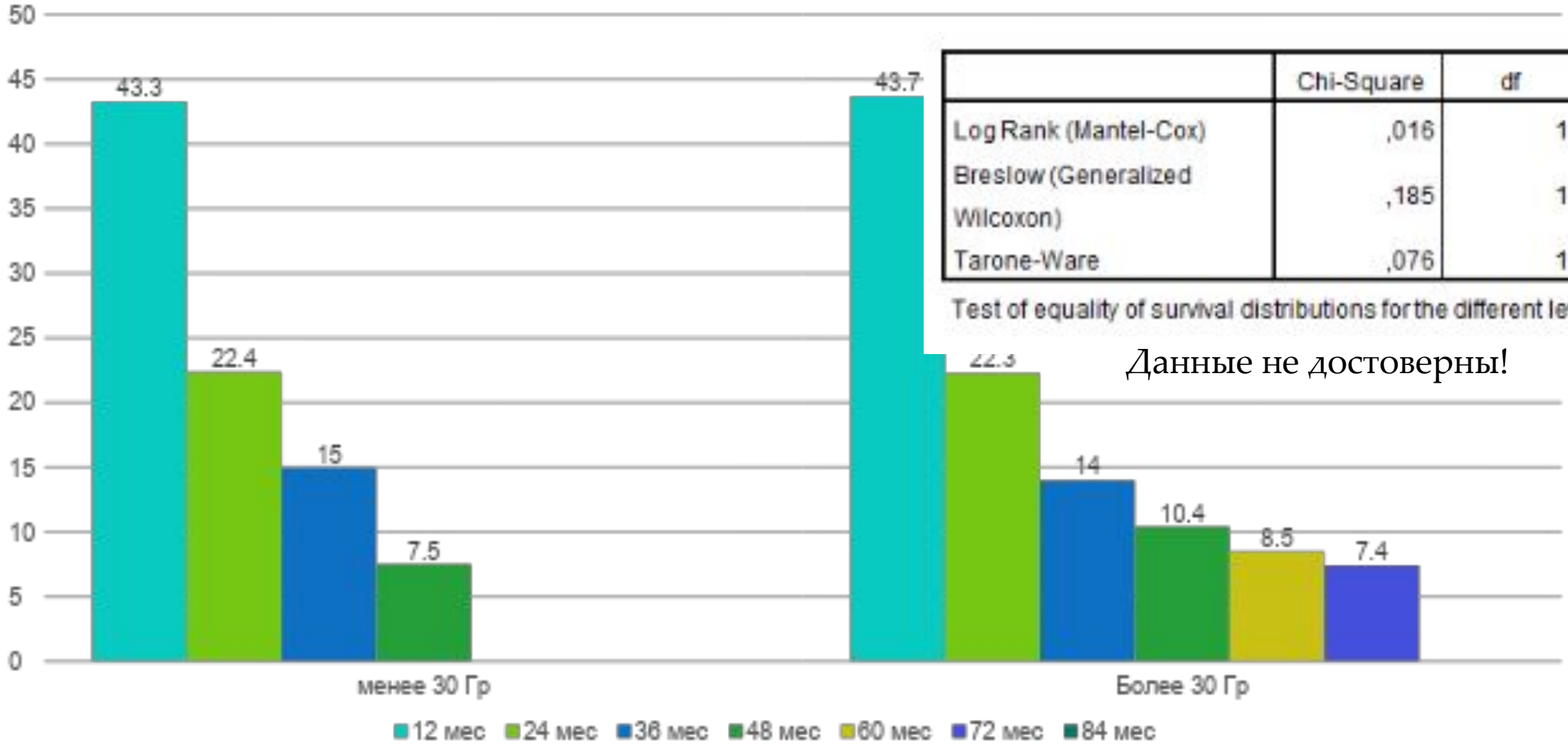


Средние значения и медианы для времени выживания

общий статус: удовл 0,неудовл 1	Среднее значение[a]					
	Оценка	Стандартная Ошибка	95% доверительный интервал		Оценка	Стандартная Ошибка
			Нижняя граница	Верхняя граница		
0	22,336	2,072	18,276	26,396	12,000	,96
1	3,185	,320	2,557	3,813	3,000	,43
Все	20,025	1,869	16,362	23,689	11,000	,94

24 мес 36 мес 48 мес 60 мес 72 мес

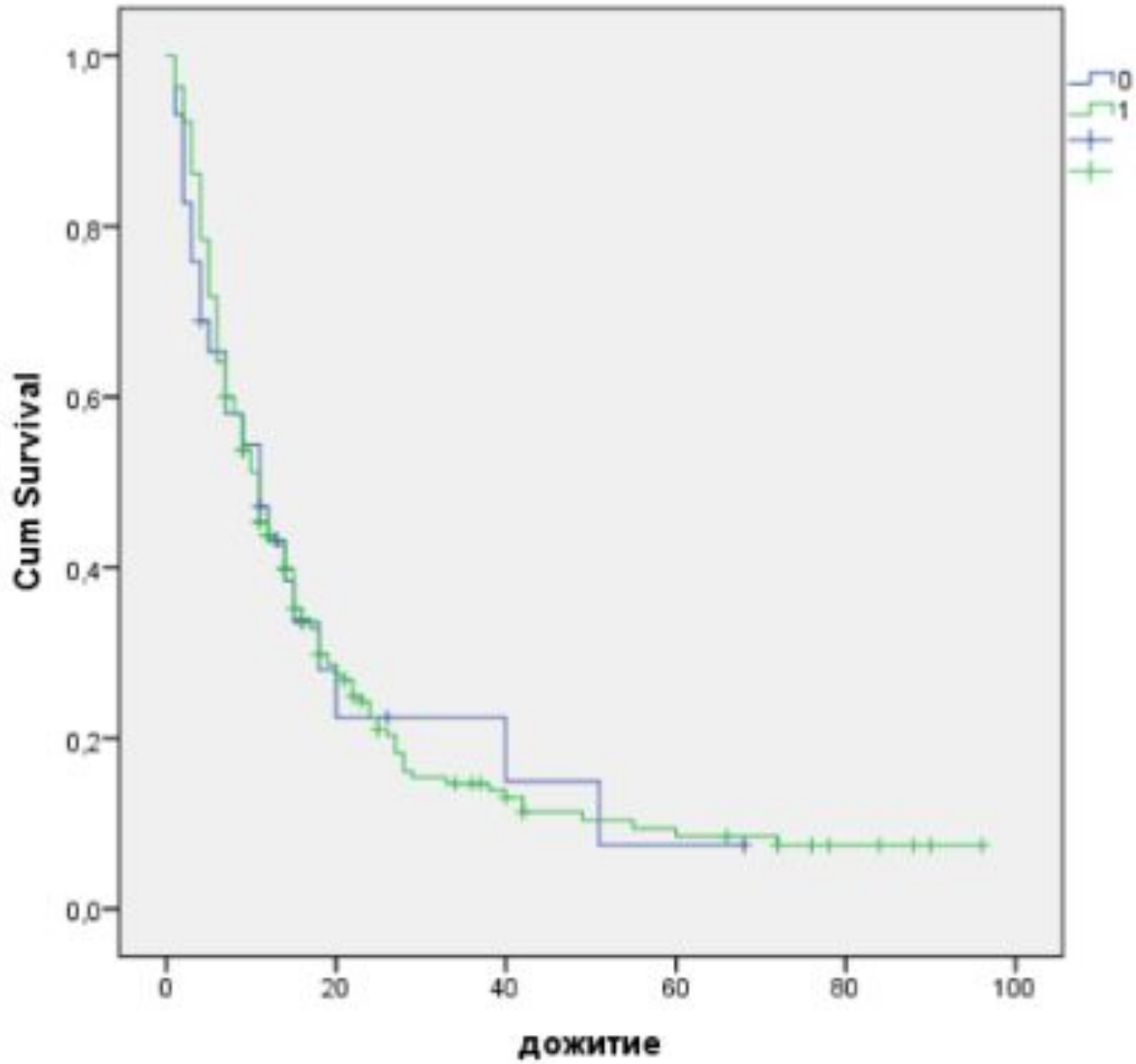
ОВ в зависимости от подведенной дозы



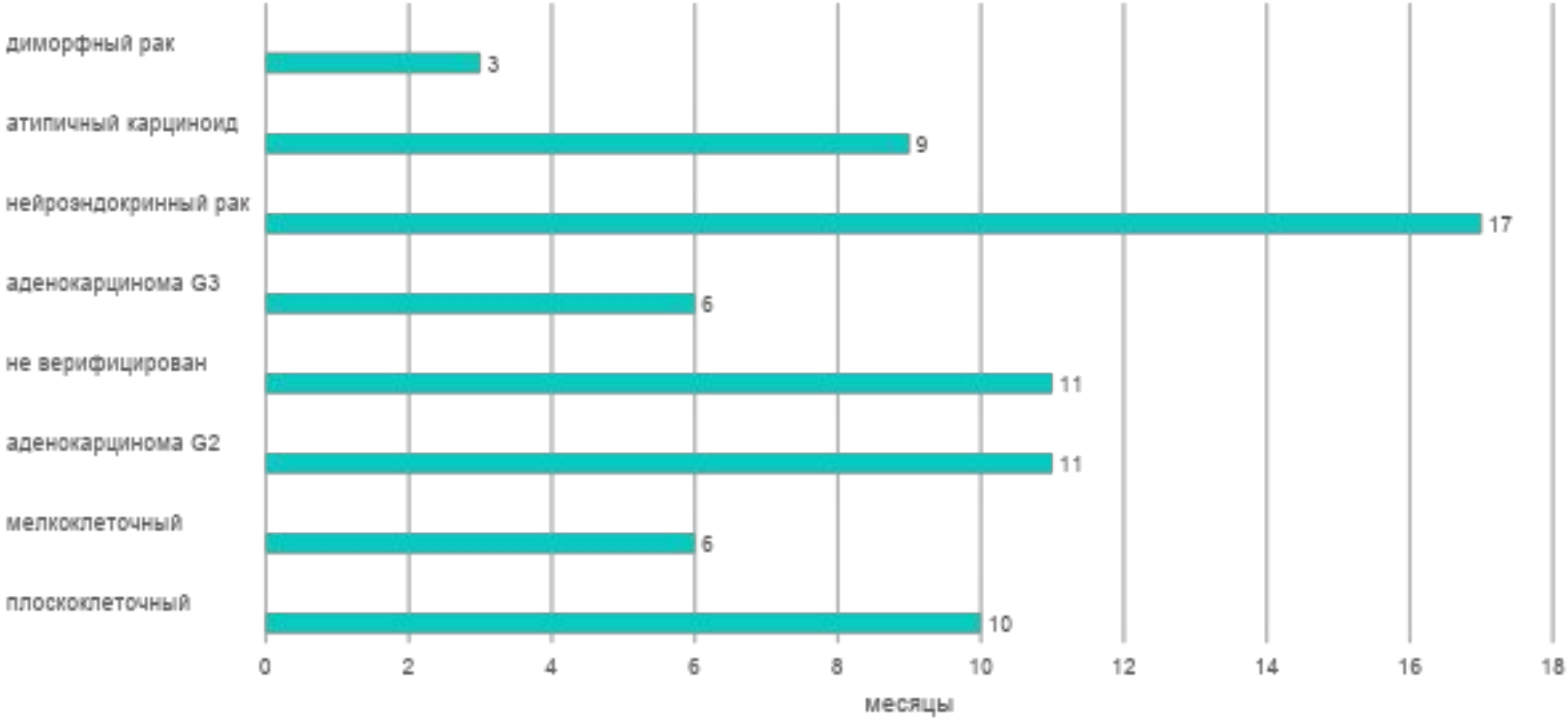
	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	,016	1	,899
Breslow (Generalized Wilcoxon)	,185	1	,667
Tarone-Ware	,076	1	,783

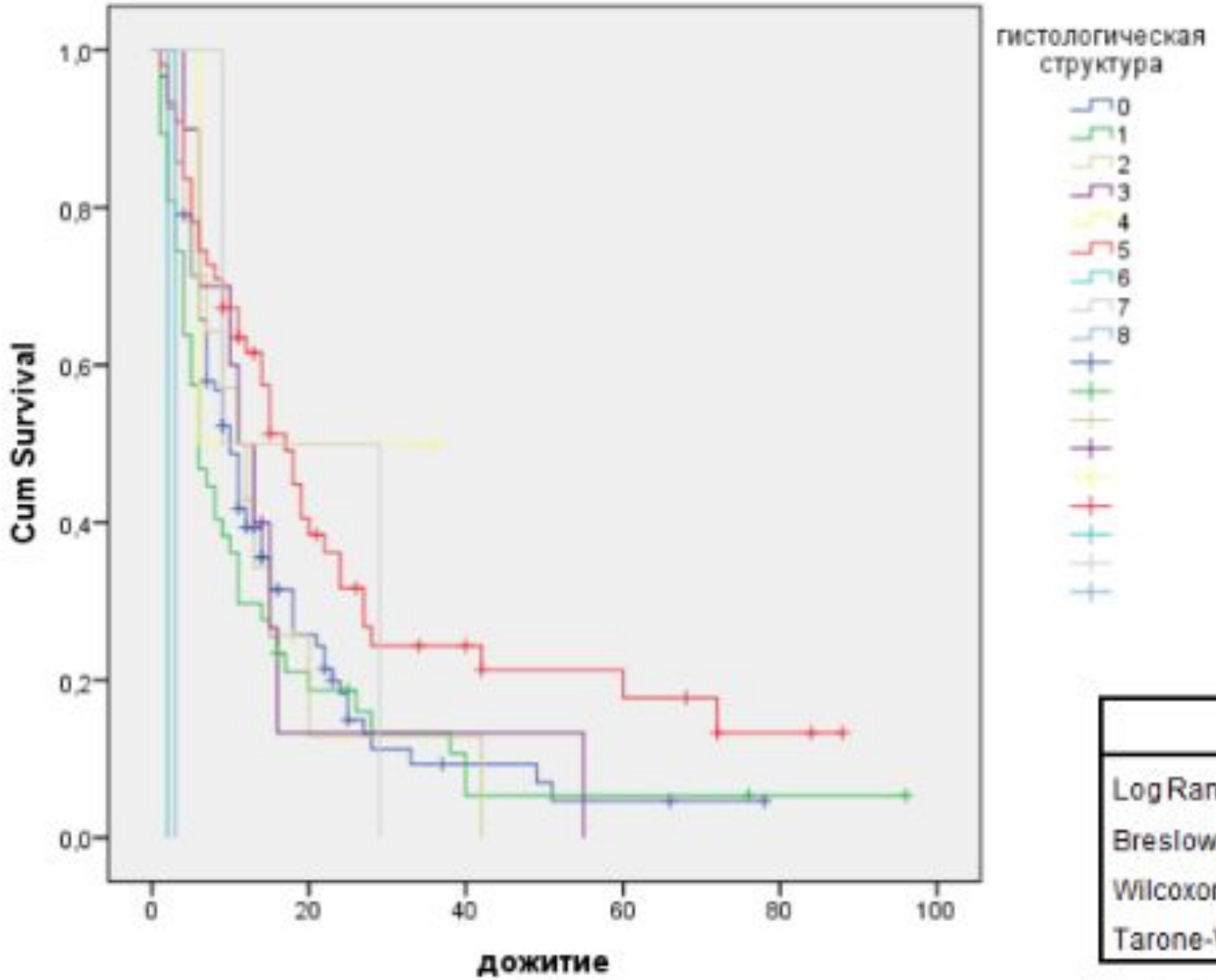
Test of equality of survival distributions for the different levels of V4.

Данные не достоверны!


Cum Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
20
40
60
80
100
дожитие
0
1

ОВ в зависимости от морфологии опухоли





Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	25,453	8	,001
Breslow (Generalized Wilcoxon)	26,562	8	,001
Tarone-Ware	26,478	8	,001

Выводы

- Для планирования проведения паллиативного курса ДЛТ необходимо оценить общий статус больного, стадию, объем облучения, наличие симптомов, которые вызваны местным распространением опухоли.
- ОВ в группе больных с СОД более 30 Гр оказалась статистически-незначимо большей, чем в группе с СОД менее 30 Гр. Это означает, что стратегии в выборе режима фракционирования в каждой конкретной клинической ситуации могут быть выбраны исходя из ряда дополнительных критериев, прежде всего общего статуса больного.
- Пациенты с удовлетворительным PS следует рассматривать как кандидатов для проведения «высокодозной» ЛТ (более 30 Гр),с учетом большей токсичности лечения, по сравнению с низкодозной.