

**ОМЛ: пришло время для
нового протокола?**

Основные вопросы

- Нужна ли высокодозная консолидация в принципе (за исключением случаев с благоприятным прогнозом), какова доза цитозара, сколько курсов?
- Можно ли обойтись без поддерживающей терапии?
- Аутологичная трансплантация???

Протокол «Kz.AML.2010»



Протокол лечения острого миелобластного лейкоза у взрослых

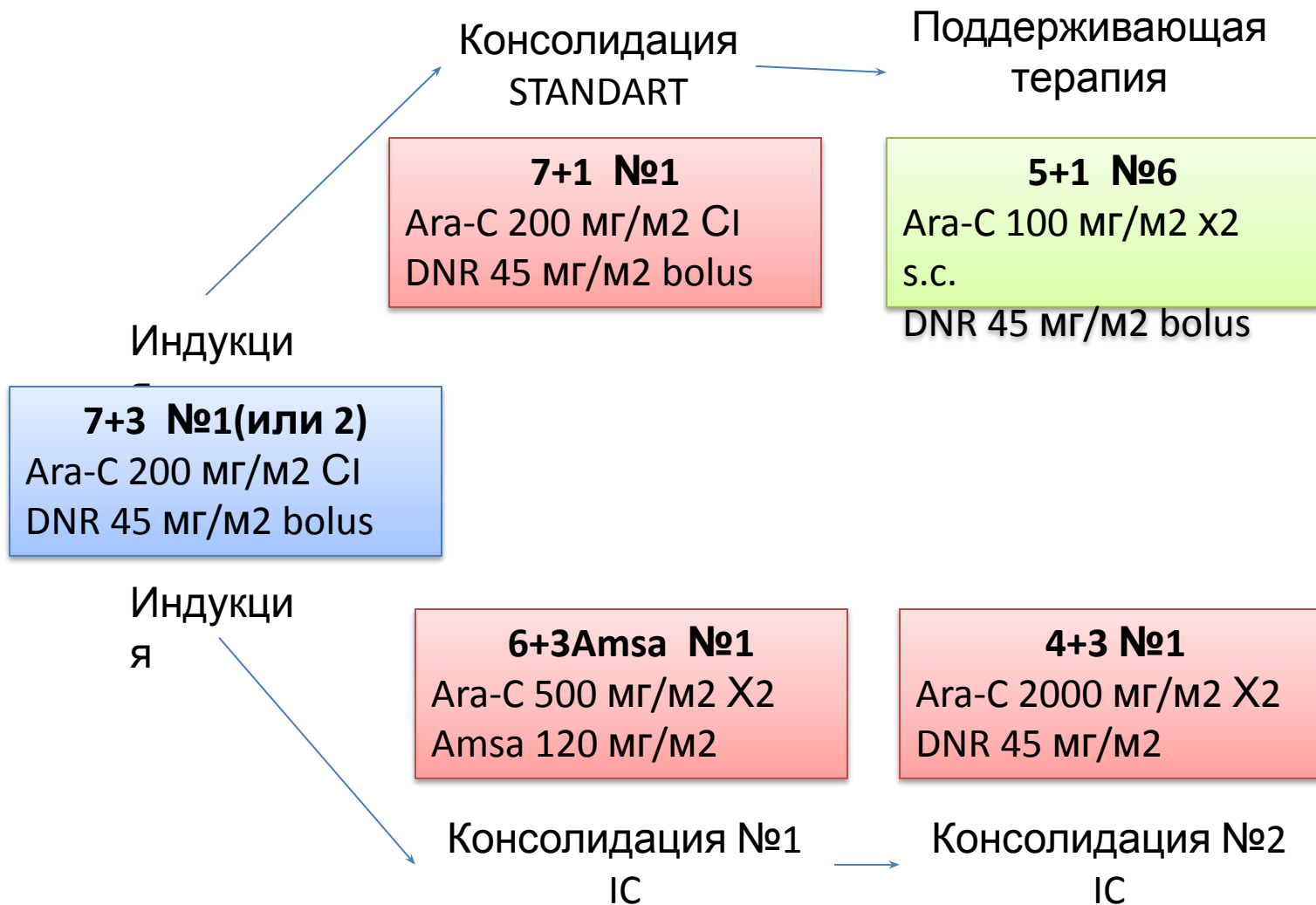


* При благоприятном прогнозе (выявление при стандартном цитогенетическом исследовании $t(8;21)(q22;q22)$, $inv(16)/t(16;16)$ и/или генов CBFB/MYH11, AML1/ETO при молекулярно-генетическом исследовании) проводится высокодозная консолидация: один курс НАМ, три курса высоких доз цитозара (3 г/м² 2 раза в день 1, 3, 5, 7 дни курса)

Intensive consolidation therapy compared with standard consolidation and maintenance therapy for adults with acute myeloid leukaemia aged between 46 and 60 years: final results of the randomized phase III study (AML 8B) of the European Organization for Research and Treatment of Cancer (EORTC) and the Gruppo Italiano Malattie Ematologiche Maligne dell'Adulto (GIMEMA) Leukemia Cooperative Groups

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Дизайн исследования



Безрецидивная выживаемость

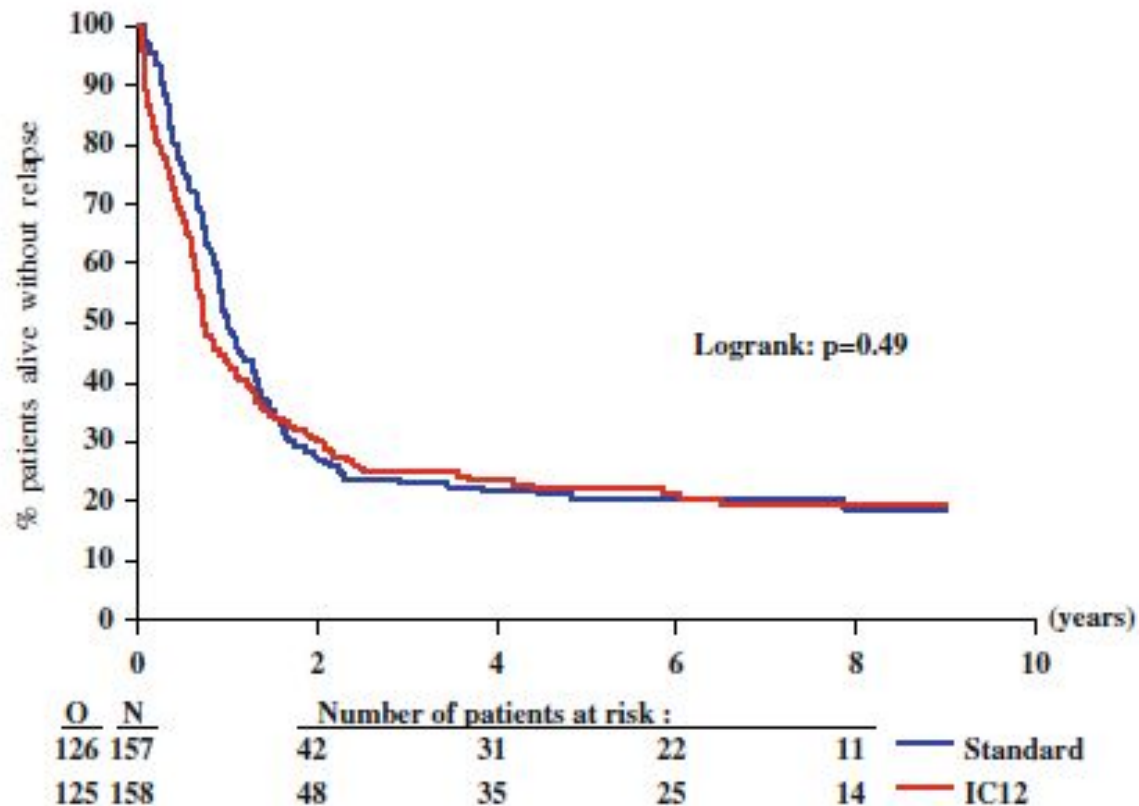


Fig. 2 Kaplan–Meier plot of relapse-free survival according to the randomized arm. *N* number of patients, *O* observed number of events (relapse or death in first complete remission), *Standard* standard consolidation and maintenance therapy, *IC12* intensive consolidation therapy

Кумулятивная инцидентность смерти в первой полной ремиссии

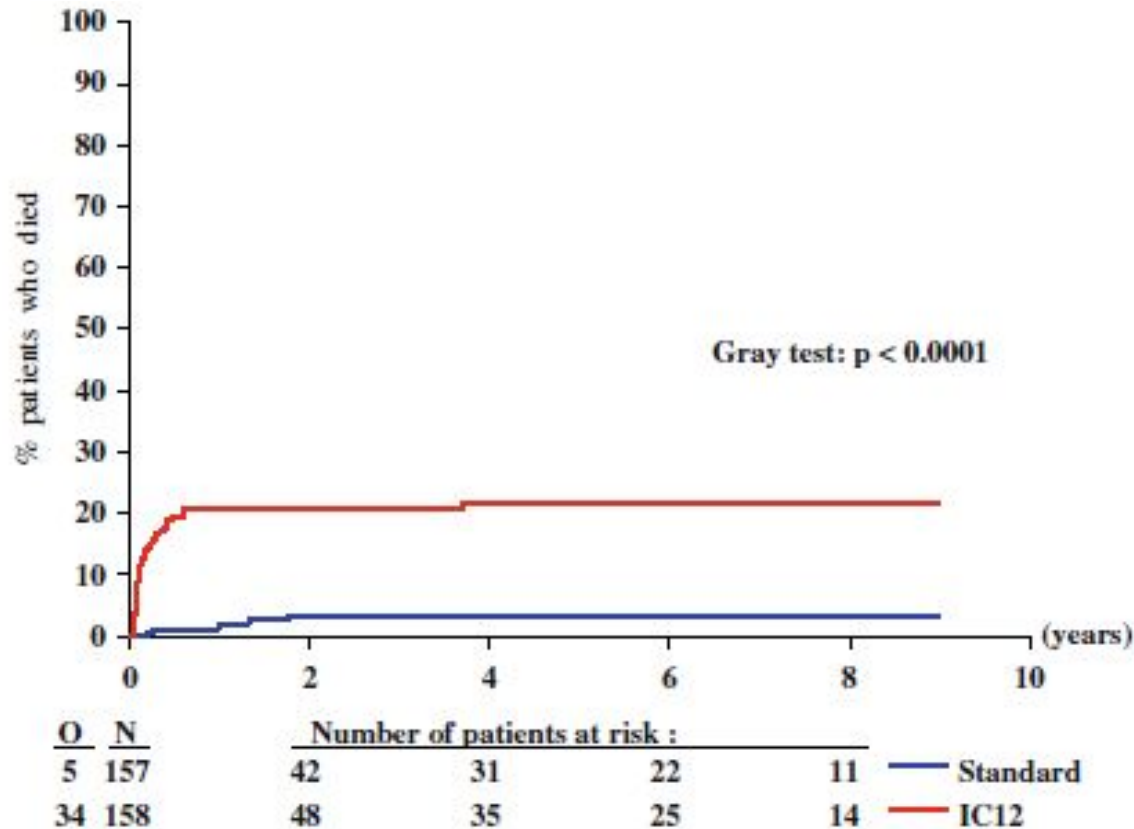


Fig. 4 Cumulative incidence of death in first complete remission according to randomized arm. *N* number of patients; *O* observed number of events (death in first complete remission), considering relapse as a competing risk; *Standard* standard consolidation and maintenance therapy; *IC12* intensive consolidation therapy

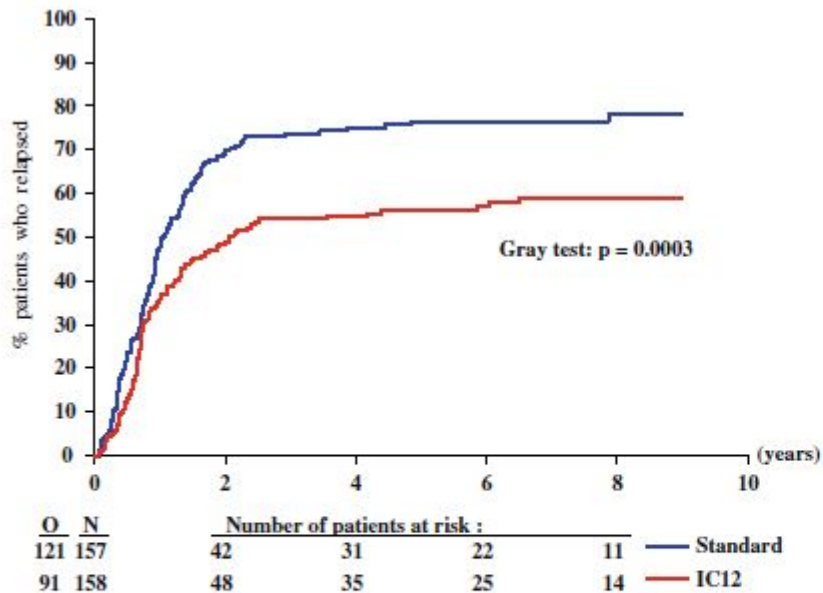


Fig. 3 Cumulative incidence of relapse according to randomized arm. *N* number of patients; *O* observed number of events (relapse), considering death in first complete remission as a competing risk; *Standard* standard consolidation and maintenance therapy; *IC12* intensive consolidation therapy

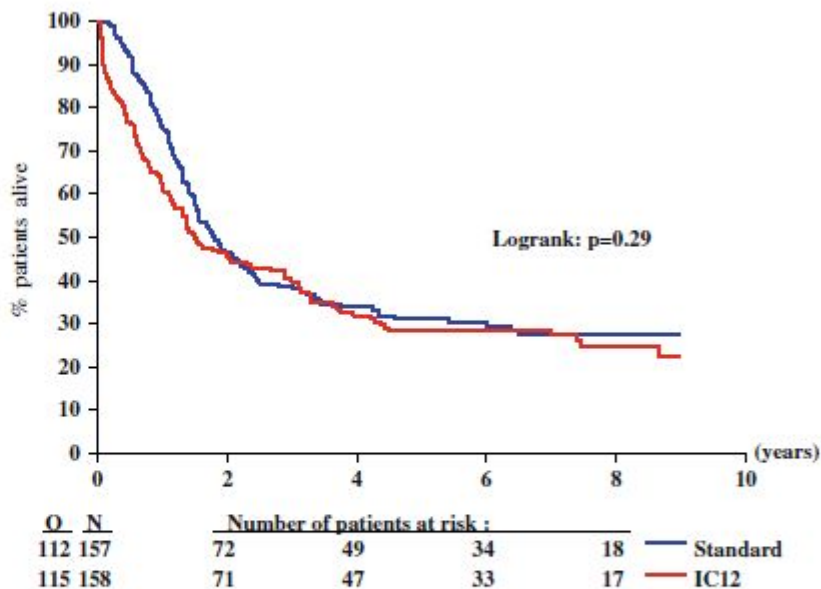


Fig. 5 Kaplan-Meier plot of survival according to the randomized arm. *N* number of patients, *O* observed number of deaths, *Standard* standard consolidation and maintenance therapy, *IC12* intensive consolidation therapy

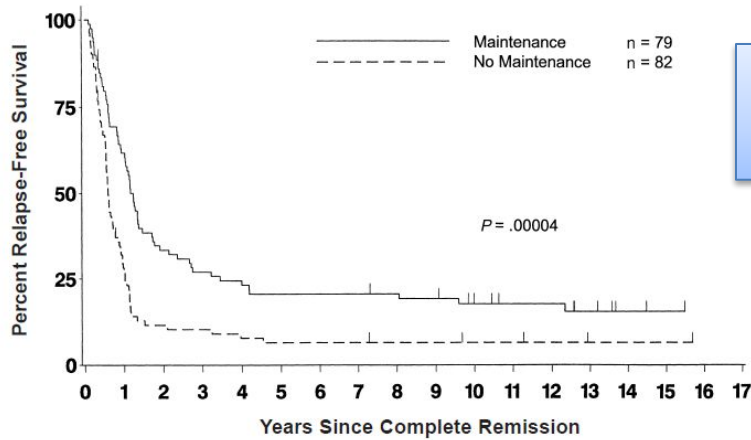
**При высокодозной консолидации в первую очередь
вероятность смерти выше у пациентов с высокой
вероятностью рецидива**

Acute Myeloid Leukemia in Adults: Is Postconsolidation Maintenance Therapy Necessary?

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Стандартная консолидаци
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Figure 1. Relapse-free survival in the 1981 AMLCG study: Patients aged 16 to 78 years received 1 to 2 courses of standard-dose 6-thioguanine-AraC-daunorubicin (TAD) for remission induction, and patients entering complete remission were randomized to receive 1 course of TAD for consolidation and no further treatment or the same consolidation followed by maintenance for 3 years. Maintenance included monthly courses of 5-day standard-dose cytosine arabinoside combined with a second drug, which rotated among daunorubicin, 5-thioguanine, or cyclophosphamide. Tick marks indicate patients alive without relapse at the most recent follow-up.

Интенсивная консолидаци
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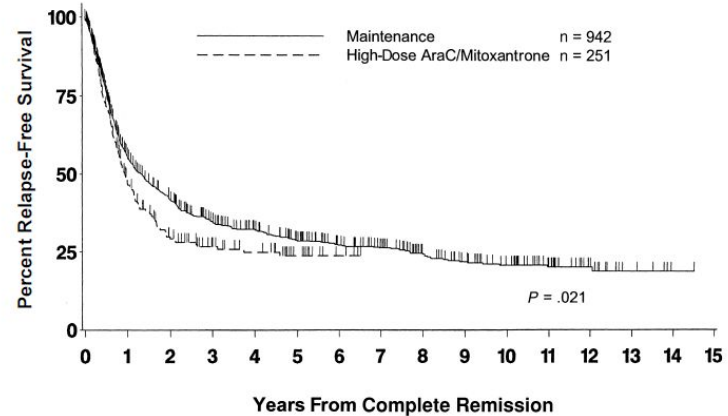


Figure 2. Relapse-free survival in the combined 1986 and 1992 AMLCG studies in patients aged 16 to 83 years. Induction treatment in patients aged <60 years was doubled with 2 courses of standard-dose TAD or TAD followed by high-dose Ara-C/mitoxantrone (HAM), and in patients aged ≥60 years, 1 to 2 courses of standard-dose TAD or HAM were used as the second course. All patients entering complete remission received 1 course of standard-dose TAD for consolidation and randomly received either 3 years of maintenance (see Figure 1) or 1 course of sequential HAM and no further treatment. Tick marks indicate patients alive without relapse at the last follow-up.

!Ротирующая схема!

Maintenance was determined by a study of Cancer and Leukemia Group B (CALGB) in which 5-day courses of standard-dose cytosine arabinoside (Ara-C) were given monthly and were combined by rotation with a second agent such as daunorubicin, 6-thioguanine (TG), or cyclophosphamide

Два пути с одинаковым результатом

- 1
 - Стандартная консолидация + поддерживающая терапия

- 2
 - Интенсивная консолидация без поддерживающей терапии

РОССИЙСКИЙ ОПЫТ

- 1992 -1995 (ОМЛ-92)
 - 7+3+VP-16, 3 года поддерживающей терапии (ротация/7+3)
 - 7+3, 3 года поддерживающей терапии
- 1995 -1999 (ОМЛ-95)
 - 7+3 (45) , 3 года поддерживающей терапии
 - 7+3 (45), 1 года поддерживающей терапии
 - 7+3 (60), 1 год поддерживающей терапии
- 2001 – 2006 (ОМЛ-01.01)
 - 7+3+VP-16 N4, 1 год поддерживающей терапии
 - 7+3+VP-16 N2, 1 год поддерживающей терапии
 - 7+3+VP-16 N2, HAD N2
- 2006 – 2009 (ОМЛ-06.06)
 - 7+3, HAM, HAM/HiDAC, HiDAC N2
 - 7+3, HAM, HAM/HiDAC, HiDAC N2, поддерживающая терапия

Результаты индукционного лечения больных ОМЛ в разных исследованиях

Показатели	Исследование			
	ОМЛ-92 (n=185)	ОМЛ-95 (n=251)	ОМЛ-01.01* (n=354)	ОМЛ-06.06 (n=109)
Полная ремиссия, % после 1 курса	63,4	61,0	Н.д.	78,0
	51,9	48,6	55,4	51,0
Резистентность,%	15,1	21,9	34,1	3,0
Ранняя летальность, %	21,5	17,1	10,5	19,0
Смерть в ремиссии,%	18,1	15,3	10,0	13,0

Долгосрочные результаты Российских клинических исследований по лечению ОМЛ

Показатели	Исследование			
	ОМЛ-92	ОМЛ-95	ОМЛ-01.01	ОМЛ-06.06
3-летняя общая / безрецидивная выживаемость, %	27 / 38	30 / 46	38 / 45	38 / 20
5-летняя общая/ безрецидивная выживаемость, %	25/ 35	25 / 28	25,5 / 25	Н.д.
7-летняя общая/ безрецидивная выживаемость, %	18 / 29,5	Н.д.	19 / 21	Н.д.

Американские рекомендации: ИНДУКЦИЯ

CLASSIFICATION

TREATMENT INDUCTION^{ii,jj}

AML^{gg,hh}

Age^{gg} <60 y

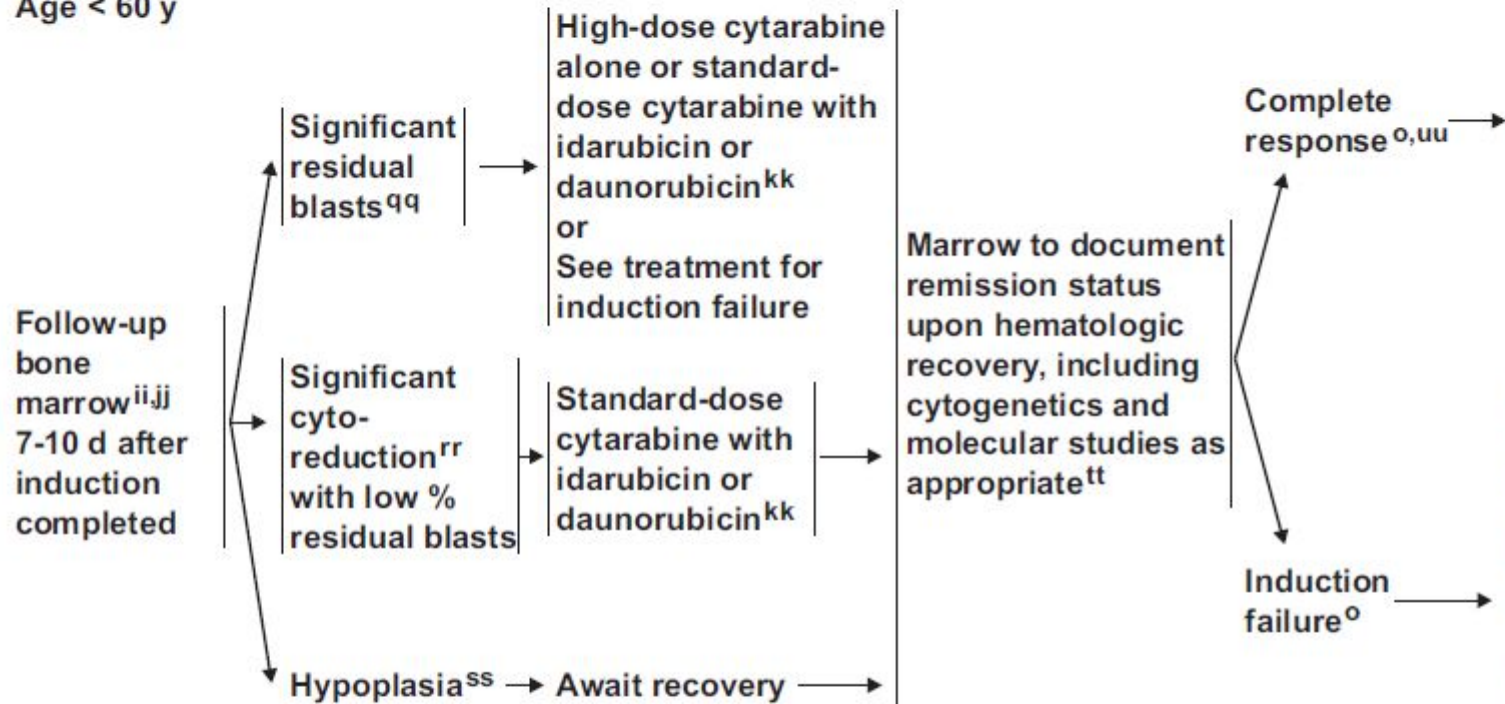
Clinical trial (preferred)
or
Standard-dose cytarabine 100-200 mg/m² continuous infusion x 7 days with idarubicin 12 mg/m² or daunorubicin 60-90 mg/m² x 3 days^{kk,ll} (category 1)
or
High-dose cytarabine (HiDAC)^{ll,mm} 2 g/m² every 12 hours x 6 daysⁿⁿ or 3 g/m² every 12 h x 4 days^{oo} with idarubicin 12 mg/m² or daunorubicin 45-60 mg/m² x 3 days (1 cycle) (category 2B)
or
Matched sibling or alternative donor HSCT^{pp} (category 2B)

DNR 60-90
МГ/М²

Американские рекомендации: ПОСИНДУКЦИОННЫЙ курс

AML POST-INDUCTION THERAPY AFTER STANDARD-DOSE CYTARABINE

Age < 60 y



Американские рекомендации: КОНСОЛИДАЦИЯ

RISK STATUS (See AML-A)

POST-REMISSION THERAPY

Better-risk
cytogenetics
or molecular
abnormalities

High-dose cytarabine 3 g/m² over 3 h every 12 h on days 1, 3, 5 × 3-4 cycles (category 1)^{ww,xx}
or
1 to 2 cycles of high-dose cytarabine-based consolidation followed by autologous HSCT^{yy} (category 2B)
or
Clinical trial

Intermediate-risk
cytogenetics
or molecular
abnormalities

Matched sibling or unrelated donor HSCT
or
High-dose cytarabine 1.5-3 g/m² over 3 h every 12 h on days 1, 3, 5 × 3-4 cycles
or
1 to 2 cycles of high-dose cytarabine-based consolidation followed by autologous HSCT
or
Clinical trial

Treatment-related
disease or poor-
risk cytogenetics
or molecular
abnormalities^{qq,vv}

Clinical trial^{zz}
or
Matched sibling or alternative donor HSCT^{aaa}
or
1 to 2 cycles of high-dose cytarabine-based consolidation followed by autologous HSCT if no allogeneic transplant option is available

Age <60

