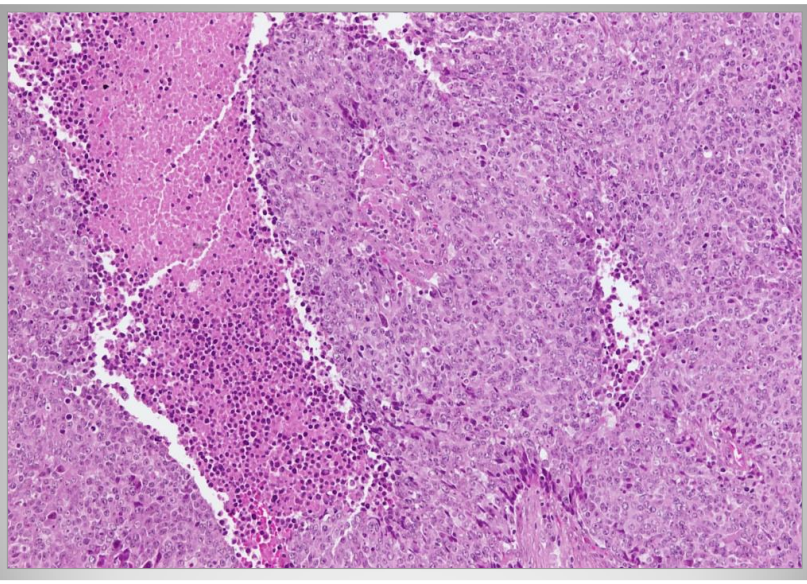
Московская Городская
Онкологическая Больница № 62
ДЕПАРТАМЕНТ ЗДРАВООХРАНЕНИЯ Г. МОСКВЫ

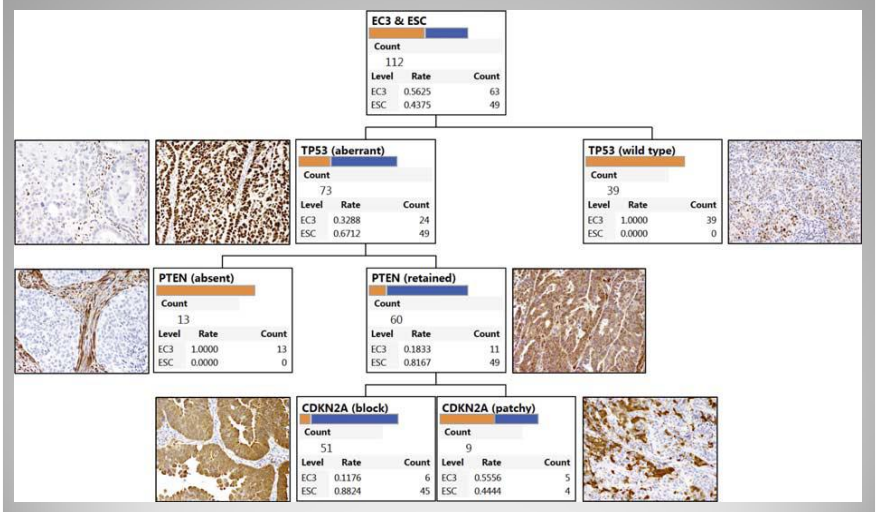
Рак эндометрия: MSI и PD-L1

Зав. ПАО Савёлов Н.А.

2021

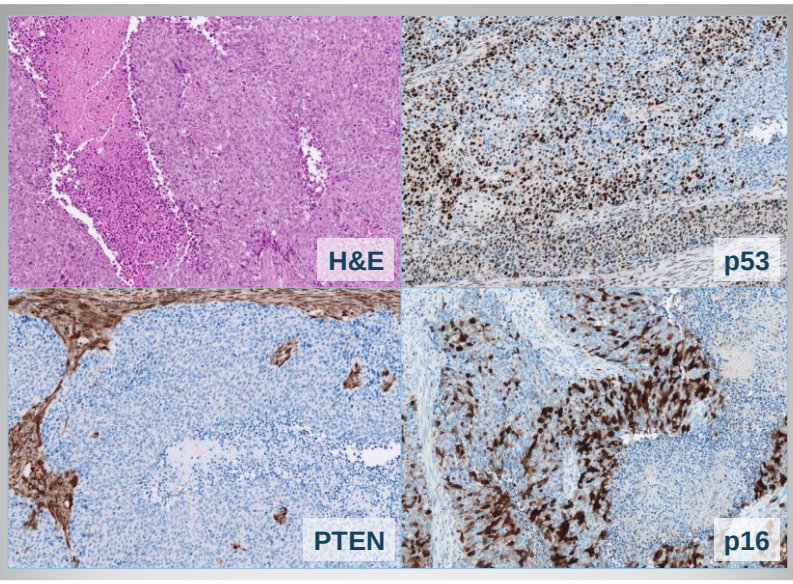


Рак эндометрия high grade



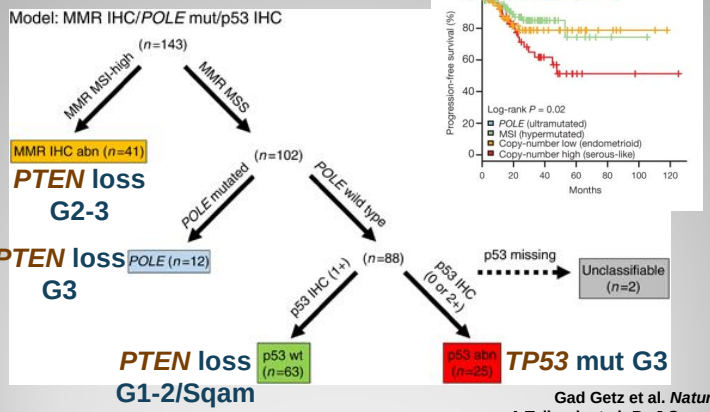
W Chen et al. *Int J Gynecol Pathol* 2013

Рак эндометрия high grade



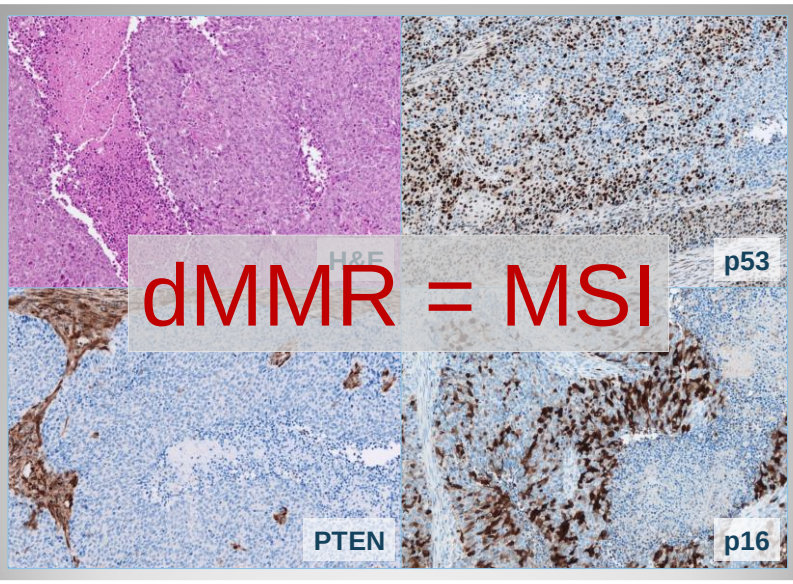
Эндометриоидная АК, но какой прогноз?

- **Мутация гена *POLE***
- **ИГХ: MLH1, PMS2, MSH2, MSH6**
- **ИГХ: p53**



Gad Getz et al. *Nature* 2013
A Talhouk et al. *Br J Cancer* 2015

Canada study: 4 типа



dMMR = MSI

Эндометриоидная АК: MSI

Risk group	Molecular classification unknown	Molecular classification known*†
Low	► Stage IA endometrioid + low-grade‡ + LVSI negative or focal	► Stage I–II ***POLEmut*** endometrial carcinoma, no residual disease ► Stage IA **MMRd/NSMP** endometrioid carcinoma + low-grade‡ + LVSI negative or focal
Intermediate	► Stage IB endometrioid + low-grade‡ + LVSI negative or focal ► Stage IA endometrioid + high-grade‡ + LVSI negative or focal ► Stage IA non-endometrioid (serous, clear cell, undifferentiared carcinoma, carcinosarcoma, mixed) without myometrial invasion	► Stage IB **MMRd/NSMP** endometrioid carcinoma + low-grade‡ + LVSI negative or focal ► Stage IA **MMRd/NSMP** endometrioid carcinoma + high-grade‡ + LVSI negative or focal ► Stage IA **p53abn** and/or non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) without myometrial invasion
High–intermediate	► Stage I endometrioid + substantial LVSI regardless of grade and depth of invasion ► Stage IB endometrioid high-grade‡ regardless of LVSI status ► Stage II	► Stage I **MMRd/NSMP** endometrioid carcinoma + substantial LVSI regardless of grade and depth of invasion ► Stage IB **MMRd/NSMP** endometrioid carcinoma high-grade‡ regardless of LVSI status ► Stage II **MMRd/NSMP** endometrioid carcinoma
High	► Stage III–IVA with no residual disease ► Stage I–IVA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) with myometrial invasion, and with no residual disease	► Stage III–IVA **MMRd/NSMP** endometrioid carcinoma with no residual disease ► Stage I–IVA **p53abn** endometrial carcinoma with myometrial invasion, with no residual disease ► Stage I–IVA **NSMP/MMRd** serous, undifferentiated carcinoma, carcinosarcoma with myometrial invasion, with no residual disease

N Concin et al. *Int J Gynecol Cancer* 2020

ESGO/ESTRO/ESP guidelines (2020)

► **To identify patients with Lynch syndrome and triage for germline mutational analysis, MMR IHC (plus analysis of MLH1 promotor methylation status in case of immunohistochemical loss of MLH1/PMS2 expression) or MSI tests should be performed in all endometrial carcinomas, irrespective of histologic subtype of the tumor (III, B).**

► **Molecular classification is encouraged in all endometrial carcinomas, especially high-grade tumors (IV, B).**

► **POLE mutation analysis may be omitted in low-risk and intermediate-risk endometrial carcinoma with low-grade histology (IV, C).**

Levels of evidence	
I	Evidence from at least one large randomized controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, expert opinions
Grades of recommendations	
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

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ESGO/ESTRO/ESP guidelines (2020)

► When molecular classification is known:
– For patients with endometrial carcinoma stage I–II, low-risk based on pathogenic POLE-mutation, omission of adjuvant treatment should be considered (III, A).
– For the rare patients with endometrial carcinoma stage III–IVA and pathogenic POLE-mutation, there are no outcome data with the omission of the adjuvant treatment. Prospective registration is recommended (IV, C).

► For p53abn carcinomas restricted to a polyp or without myometrial invasion, adjuvant therapy is generally not recommended (III, C).

► Anti-PD1-based immune therapy with pembrolizumab could be considered for second-line therapy of MSI/MMRd carcinomas. The combination of pembrolizumab and the multi-tyrosine-kinase inhibitor lenvatinib could be considered for second-line treatment of microsatellite-stable carcinomas (III, B).

However, its use may be limited due to regulatory approvals or reimbursement in different countries. Clinical trial participation should be offered to all patients with relapse disease (V, B).

N Concin et al. *Int J Gynecol Cancer* 2020

ESGO/ESTRO/ESP guidelines (2020)