

SÚČASNOSŤ A BUDÚCNOSŤ LIEČBY MBC NA SLOVENSKU

26.-27.09.2024



HOTEL PARTIZÁN, TÁLE



SÚČASNOSŤ A BUDÚCNOSŤ

Viscerálna kríza

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Vyhlásenie o konflikte záujmov autora

Nemám potenciálny konflikt záujmov

Deklarujem nasledujúci konflikt záujmov

Forma finančného prepojenia	Spoločnosť
Participácia na klinických štúdiách/firemnom grante	
Nepeňažné plnenie (v zmysle zákona)	
Prednášajúci	
Akcionár	
Konzultant/odborný poradca	
Ostatné príjmy (špecifikovať)	

Podľa UEMS (upravené v zmysle slovenskej legislatívy)

Čo je to „viscerálna kríza“

- Orgánové zlyhávanie
- Hroziacie (?) orgánové zlyhanie
- ABC 5 konsenzus (2020):

Visceral crisis is defined as severe organ dysfunction, as assessed by signs and symptoms, laboratory studies and rapid progression of disease. Visceral crisis is not the mere presence of visceral metastases but implies important organ compromise leading to a clinical indication for the most rapidly efficacious therapy.

Examples: **Liver visceral crisis**: rapidly increasing bilirubin >1.5x ULN in the absence of Gilbert's syndrome or biliary tract obstruction. **Lung visceral crisis**: rapidly increasing dyspnoea at rest, not alleviated by drainage of pleural effusion.

Expert
opinion/n/a

97%

Konsenzus franc. onkológov

	Consensual items		Nonconsensual items
	IS A VISCERAL CRISIS	IS NOT A VISCERAL CRISIS	
GENERAL STATE		Uncontrolled pain despite the use of grade III analgesics	Deterioration of the general state
LUNG	Symptomatic lymphangitis carcinomatosis	Asymptomatic lymphangitis carcinomatosis	
	Superior vena cava syndrome	Asymptomatic pleural effusion	
		Pleural effusion with functional consequences before drainage	Pleural effusion with functional consequences despite drainage / requiring repeated drainage
	Symptomatic lung involvement	Asymptomatic pulmonary lesion, at risk of becoming symptomatic	
LIVER - ABDOMEN	High liver tumor burden, defined as a percentage of the parenchyma	Asymptomatic liver lesion, at risk of becoming symptomatic	The cutoff percentage defining high liver tumor burden
	Peritoneal carcinosis with pain and occlusion not responding to medical treatment	Asymptomatic peritoneal carcinosis	Peritoneal carcinosis with pain and occlusion responding to medical treatment
		Asymptomatic ascites	
		Ascites with functional consequences before drainage	Ascites with functional consequences despite drainage / requiring repeated drainage
	Biological hepatic dysfunction, defined as cytolysis > 5N (grade III CTCAE) and / or hyperbilirubinemia	Reversible hyperbilirubinemia after drainage	The cutoff value of hyperbilirubinemia defining hepatic dysfunction

	Consensual items		Nonconsensual items
	IS A VISCERAL CRISIS	IS NOT A VISCERAL CRISIS	
BRAIN - SPINE		Asymptomatic brain lesion(s)	Brain lesion(s) threatening functional prognosis / symptomatic, before or after local treatment
		Asymptomatic epidural involvement	
		Symptomatic epidural involvement before medical and local treatment	Epidural involvement threatening functional prognosis / symptomatic despite treatment
SKELETON		No consideration of bone tumor burden	
		Bone lesion threatening functional prognosis	
		LDH elevation > 1,5N	
		Severe hypercalcemia of malignancy, before hyperhydration and bisphosphonate	Severe hypercalcemia of malignancy, not responding to medical treatment
		Cytopenia with functional consequence(s)	Cytopenia(s) requiring repeated transfusions
		Grade 4 CTCAE cytopenia(s)	Grade 2 / 3 CTCAE cytopenia(s)
		Grade 1 CTCAE cytopenia(s)	Relevance of the number of cytopenias

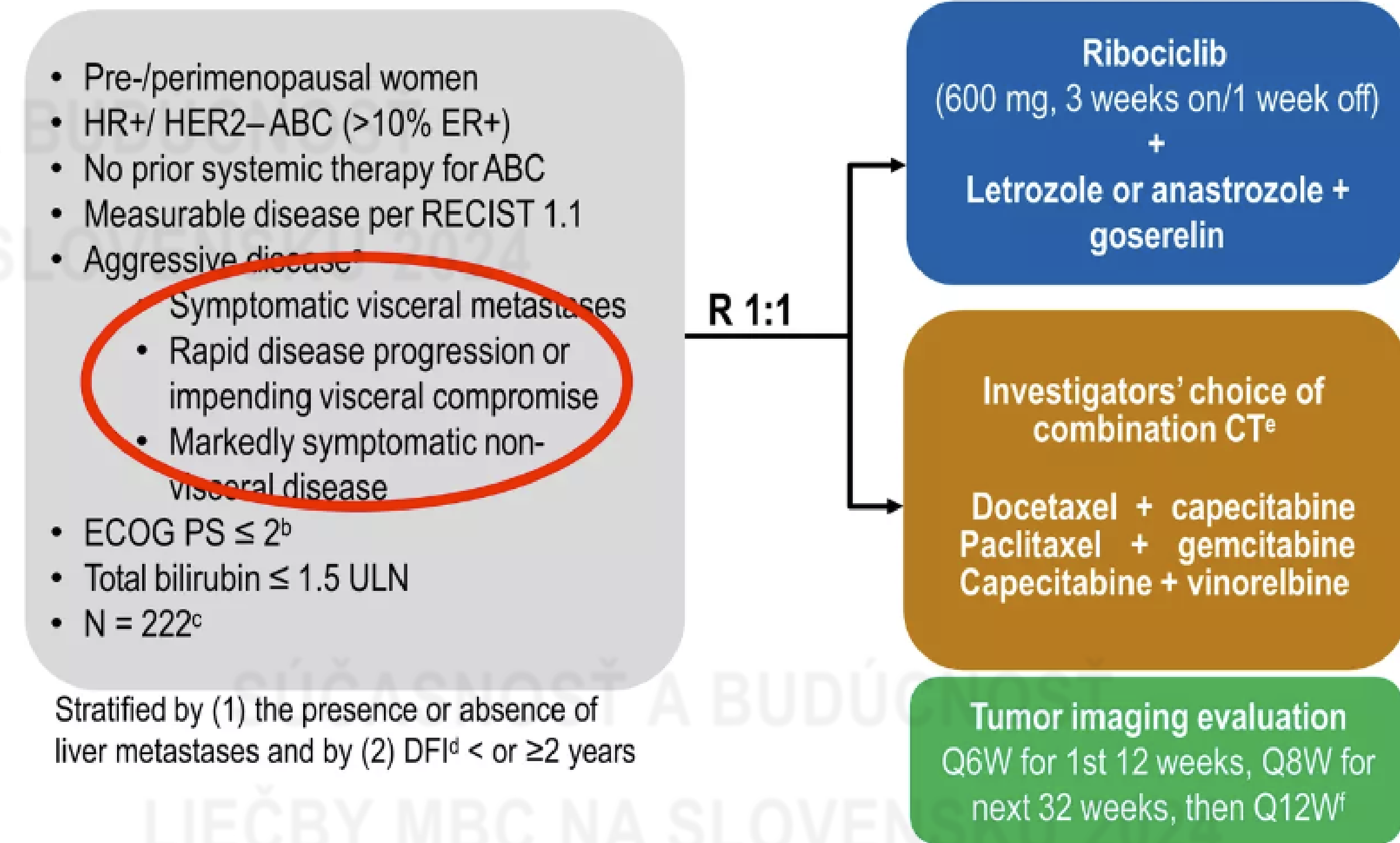
CONCLUSION

To our knowledge, this is the **first study** aiming to define VC in luminal ABC using specific clinical situations. We present here the consensual items after the two questionnaires. The remaining non-consensual items will be discussed during a final face to face expert meeting, to be held in the spring of 2023. The acquired definition could **help the clinician in his daily practice** and become a base for the **inclusion and exclusion criteria** of clinical trials.

Nabeth et al. Ann Oncol (2023) 8 (1suppl_4): 101223
doi:
10.1016/esmooop/esmooop101223

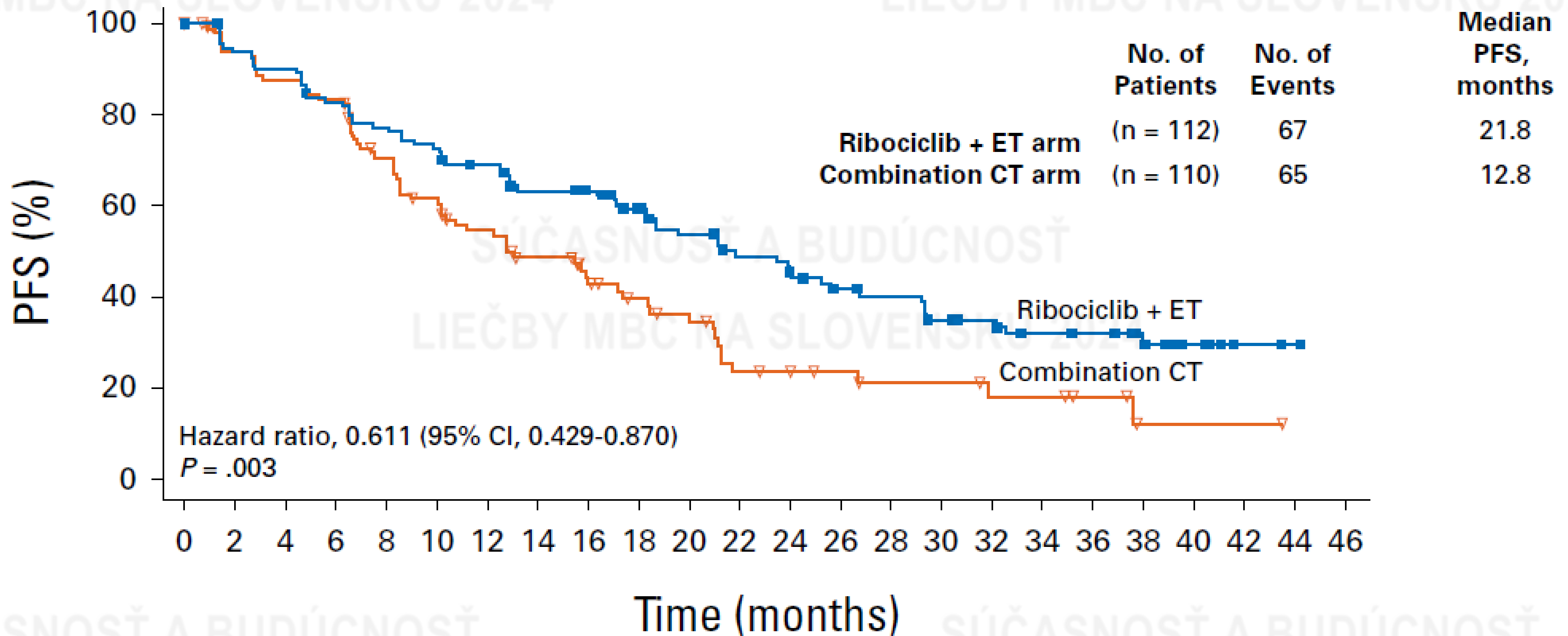
Liečba - klinické štúdie

- Štúdie spĺňajúce ABC5 definíciu
 - žiadne
- Štúdie s pac. s high-burden / aggressive disease
 - **RIGHT Choice trial** (agresívne ochorenie), fáza II
 - HR+/HER2 – pre/perimenopauzal pac.
 - Ribo/AI/LHRH vs dual chemo (TX, GP, NX)
 - 68% symptomatické visc. ochorenie
 - 48% „investigator-assessed“ visceral crisis



RIGHT Choice trial

A



No. at risk

Ribociclib + ET arm	112	103	99	90	84	79	73	65	63	55	48	41	39	32	30	25	23	19	17	13	6	2	1	0
Combination CT arm	110	90	84	79	63	54	46	38	29	24	21	13	12	10	8	8	6	6	4	1	1	1	0	0

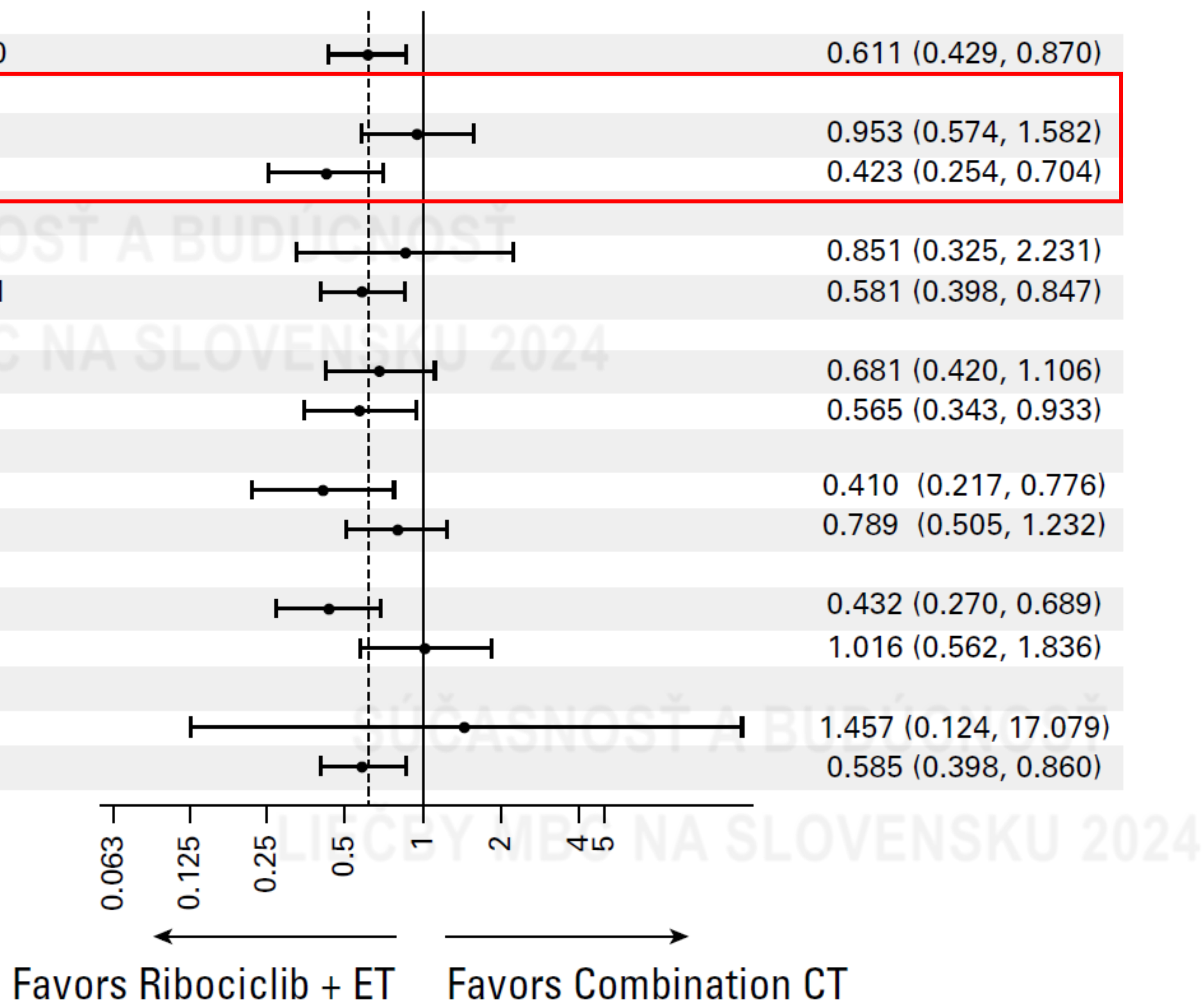
RIGHT Choice trial

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Subgroup	Ribociclib + ET Arm n/N	Combination CT Arm n/N	Hazard Ratio (95% CI)
All patients	67/112	65/110	0.611 (0.429, 0.870)
Visceral crisis status (yes v no)			
Yes	37/57	27/49	0.953 (0.574, 1.582)
No	30/55	38/61	0.423 (0.254, 0.704)
Disease-free interval, years			
<2	11/14	8/9	0.851 (0.325, 2.231)
≥2	56/98	57/101	0.581 (0.398, 0.847)
Presence of liver metastasis (yes v no)			
Yes	35/54	32/53	0.681 (0.420, 1.106)
No	32/58	33/57	0.565 (0.343, 0.933)
Age, years			
<40	19/32	28/38	0.410 (0.217, 0.776)
≥40	48/80	37/72	0.789 (0.505, 1.232)
De novo (yes v no)			
Yes	36/70	45/73	0.432 (0.270, 0.689)
No	31/42	20/37	1.016 (0.562, 1.836)
Estrogen receptor status			
<50	4/8	3/4	1.457 (0.124, 17.079)
≥50	57/95	56/96	0.585 (0.398, 0.860)



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RIGHT Choice trial

- NÚ
 - Približne rovnaké
 - Viac hematolog. NÚ na CDK4/6i ramene
 - Viac infekčných komplikácií na CHT
 - Viac ukončenia liečby pre AE na CHT (27% vs 6%)

These results reinforce the place of ET + CDK4/6 inhibitors as standard of care for 1st line therapy for the majority of patients with ER+/HER2 negative ABC, including those with “clinically aggressive disease”.

Although the trial was performed only in pre/peri-menopausal women, the panel believes the results also apply to post-menopausal women and men with the same disease characteristics.

I/A

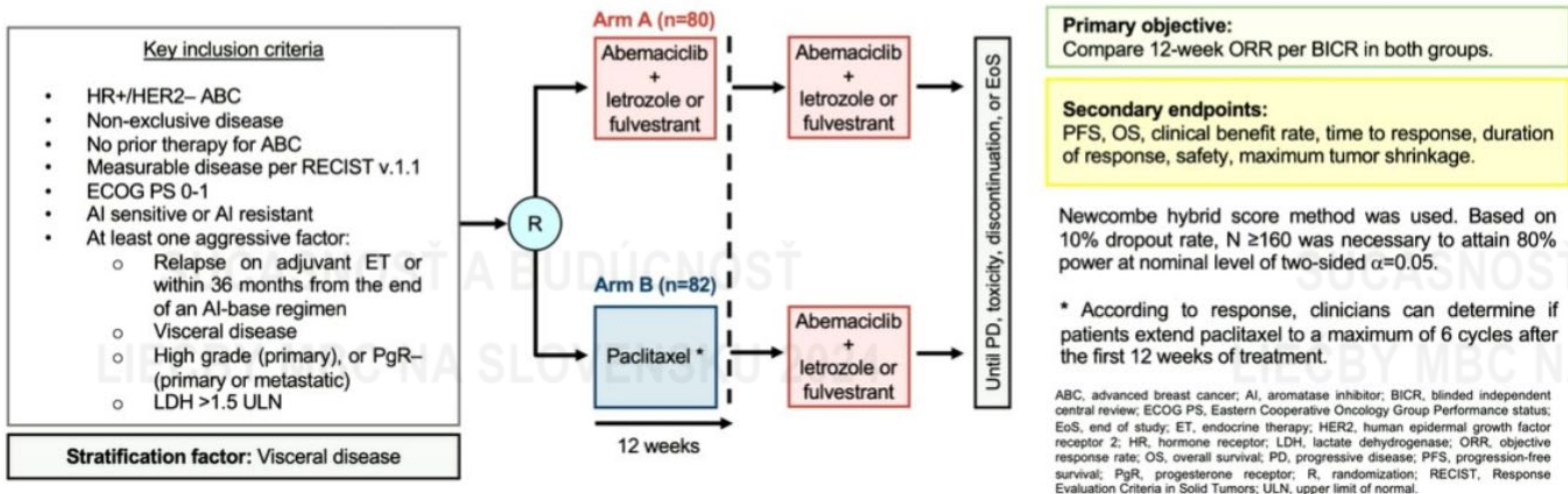
95%

Expert Opinion/B

95%

ABIGAL trial

- ER+, HER2 – pac., fáza II, nepredliečené pac.
- „Agresívne ochorenie“, PS 0-1
- ET+abema vs paklitaxel
- **ORR 59% vs 40%**



Retrospektívne štúdie

- Chemoterapia

- 35 pac. (Maroko)
- Po 2.líniach ET
- PS 2 a 3, zlyhanie pečene, LM infiltrácia, respiračné zlyhávanie, ...
- 1 cyklus chemo, mOS 4,7 týždňa (!) – rovnaké ako u BSC

- 44 pac. (Japonsko)
- 68% novoDg.
- PS 0-2, visc. kríza + hroziaca visc. kríza
- wP + bevacizumab
- mOS 10m (u PS2 5m)

Sbitti et al. World J Oncol. 2017 Aug; 8(4): 105

doi: 10.14740/wjon1043w

Funasaka et al. Breast. 2021 :58:50

doi: 10.1016/j.breast.2021.04.001

Retrospektívne štúdie

- Chemoterapia

- 261 pac. (Belgicko)
- Predliečení pac.
- Platinová chemo, mOS 3,7m
- 42% pac. ešte dostalo CHT 30d pred exitom (!)

- CDK4/6i

- 336 pac (z databázy)
- Pridanie CDK4/6i u 18%
- Zlepšenie OS z 6 na 11m

Franzoi et al. Breast. 2021;57:86-94

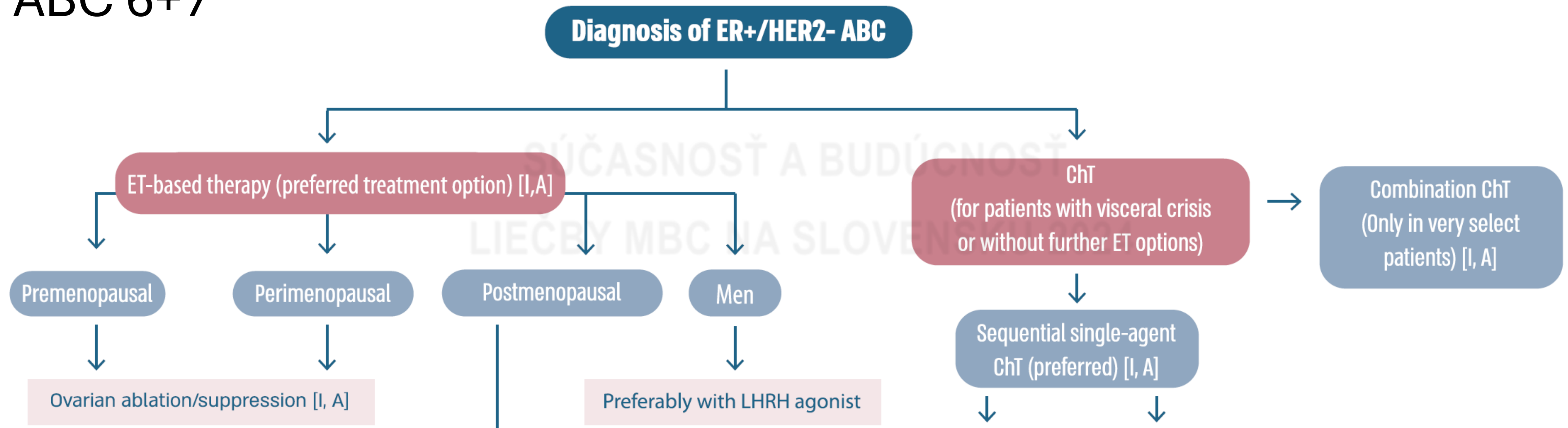
doi: 10.1016/j.breast.2021.03.002

Shaheenah et al. JCO 2021;39, 15_suppl

doi: 10.1200/JCO.2021.39.15_suppl.1047

ER+HER2 - ochorenie

- ABC 6+7



In ER+/HER2 negative ABC with visceral crisis, ET + CDK4/6 inhibitor are not contraindicated and may be a better option than chemotherapy.

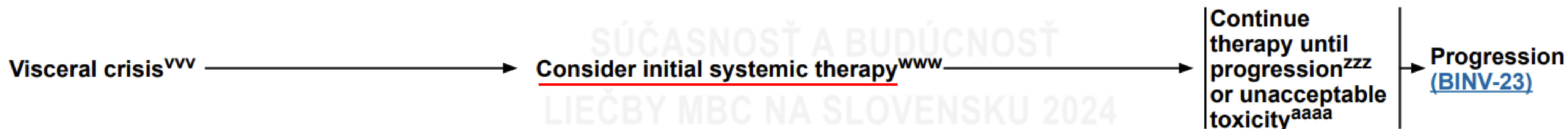
II/B

95%

ER+HER2 - ochorenie

- NCCN v 4.2024

SYSTEMIC TREATMENT OF RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE: ER- AND/OR PR-POSITIVE; HER2-NEGATIVE^d



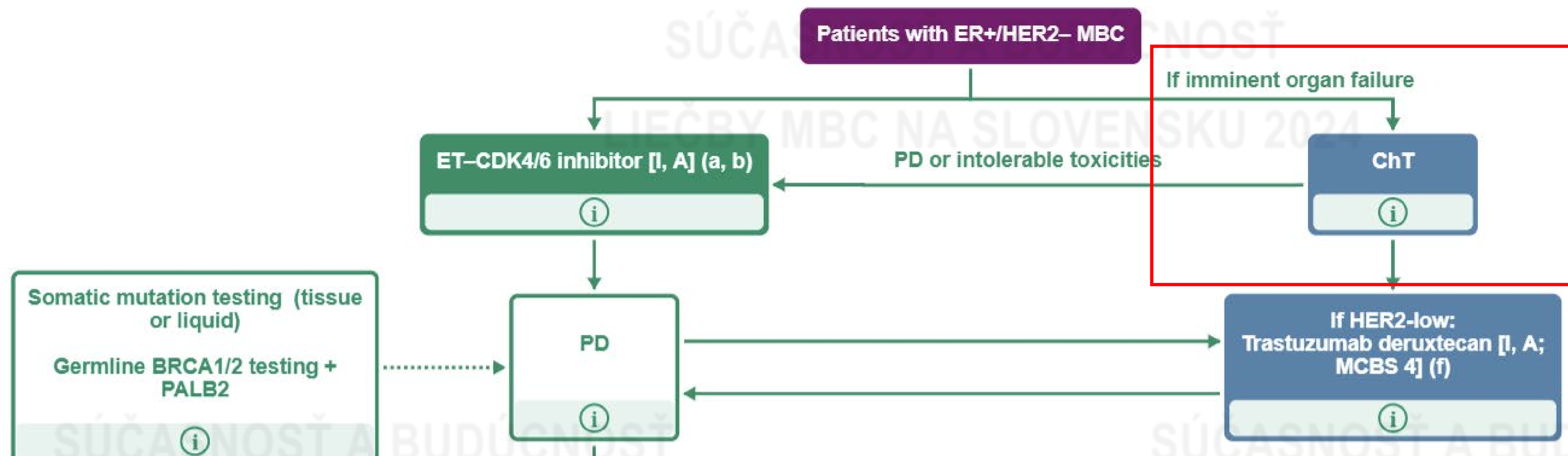
SYSTEMIC THERAPY REGIMENS FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE^a

HR-Positive and HER2-Negative with Visceral Crisis [†] or Endocrine Refractory		
Setting	Subtype/Biomarker	Regimen
First Line	No germline <i>BRCA1/2</i> mutation ^b	Systemic <u>chemotherapy</u> BINV-Q (5)
	Germline <i>BRCA1/2</i> mutation ^b	PARPi (olaparib, talazoparib) ^c (Category 1, preferred)

ER+HER2 - ochorenie

- ESMO Breast living guidelines 5/2023

v1.1 - May 2023



HER 2+ a TNBC

- HER 2+

- Maximalizovať RR
- Duálna anti-HER2 blokáda + chemo
 - Taxán + trastuzumab + pertuzumab
- ADC

In HER2+ ABC with visceral crisis, the use of anti-HER2 agents is crucial and feasible.

II/A

95%

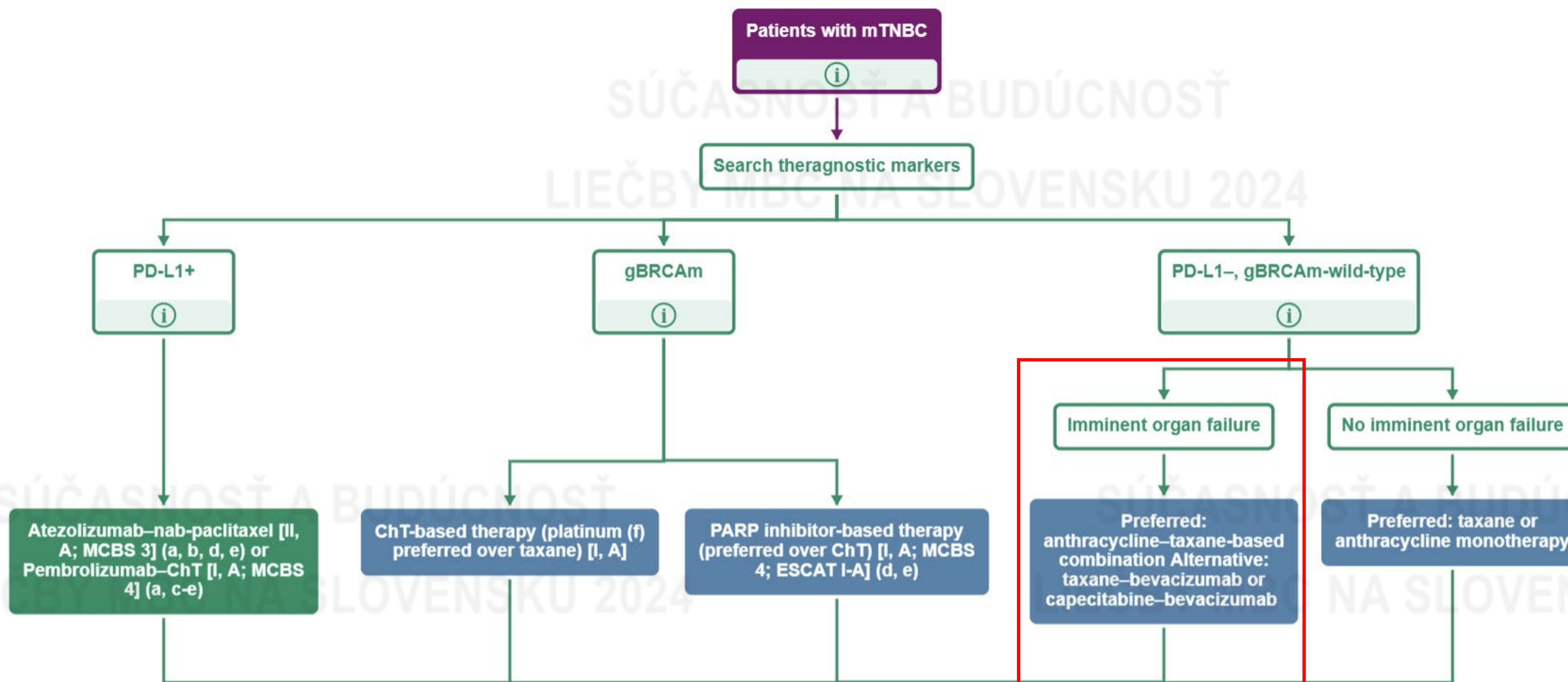
- TNBC

- CHT +/- PDL-1
- BRCA mut - PARPi, platinové preparáty

TNBC

- ESMO Breast living guidelines 5/2023

v1.1 - May 2023



Záver do praxe

- ER+ ochorenie
 - HT + CDK4/6i
- HER2+
 - Chemo + duálna antiHER2 blokáda
- Hepatálne zlyhávanie
 - Bi > 25 mmol/l - weekly, red. dávky, eskalovať dľa stavu (klinika, bioch)
 - Bi > 35 mmol/l – kapecitabíne, platina...
- Zlyhanie KD
 - Weekly paklitaxel, kapecitabine (X-7/7)
 - HT + CDK4/6i

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Ďakujem za pozornosť

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