Lymphome de Hodgkin avancé en 1°ligne

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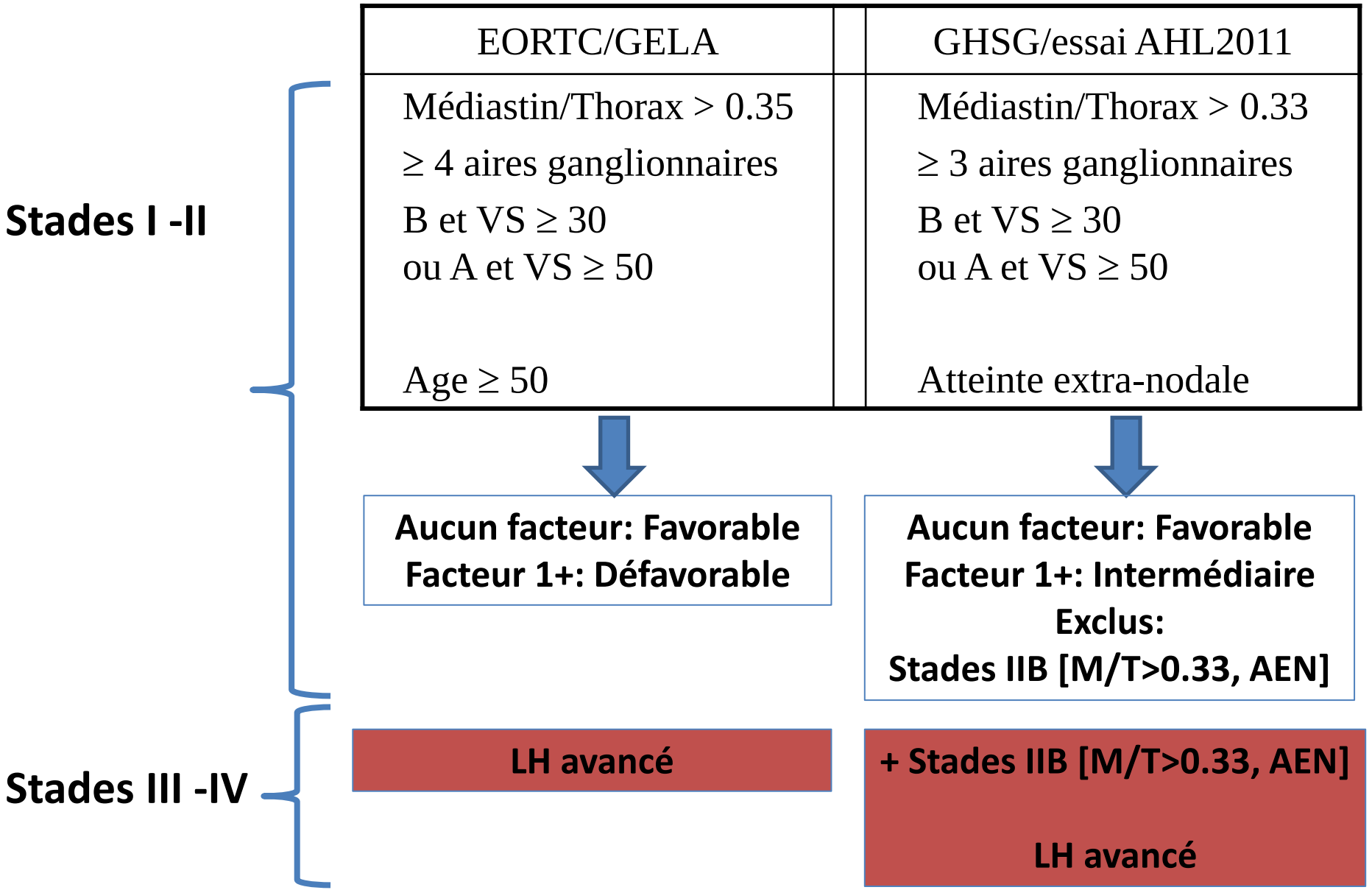
Stratification



La TEP modifie-elle la prise en charge initiale?

		n	Δ Stade (%)	Δ management (%)
Shah (2000)	LNH/LH	29	-	31
Raannani (2005)	LNH/LH	103	36	45
Hernandez (2006)	LNH/LH	47	23	15
Naumann (2004)	LH	88	20	18
Hutchings (2006)	LH	30	-	33
Rigacci (2007)	LH	186	16	-

Schémas de polychimiothérapie: les 2 champions

1975

ABVD regimen	Dose	D1	D15
Doxorubicin	25 mg/m² (IV)	X	X
Bleomycin	10 mg/m² (IV)	X	X
Vinblastine	6 mg/m² (IV)	X	X
Dacarbazine	375 mg/m² (IV)	X	X

1993

BEACOPPesc regimen	Dose	D1	D2	D3	D4	D5	D6	D7	D8	D9 to D14
Bleomycin	10 mg/m² (IV)								X	
Etoposide	200 mg/m² (IV)	X	X	X						
Doxorubicin	35 mg/m² (IV)	X								
Cyclophosphamide	1250 mg/m² (IV)	X								
Vincristine	1,4 mg/m² (IV) [2mg max]								X	
Procarbazine	100 mg/m² (PO)	X	X	X	X	X	X	X		
Prednisone	40 mg/m²(PO)	X	X	X	X	X	X	X	X	X

ABVD

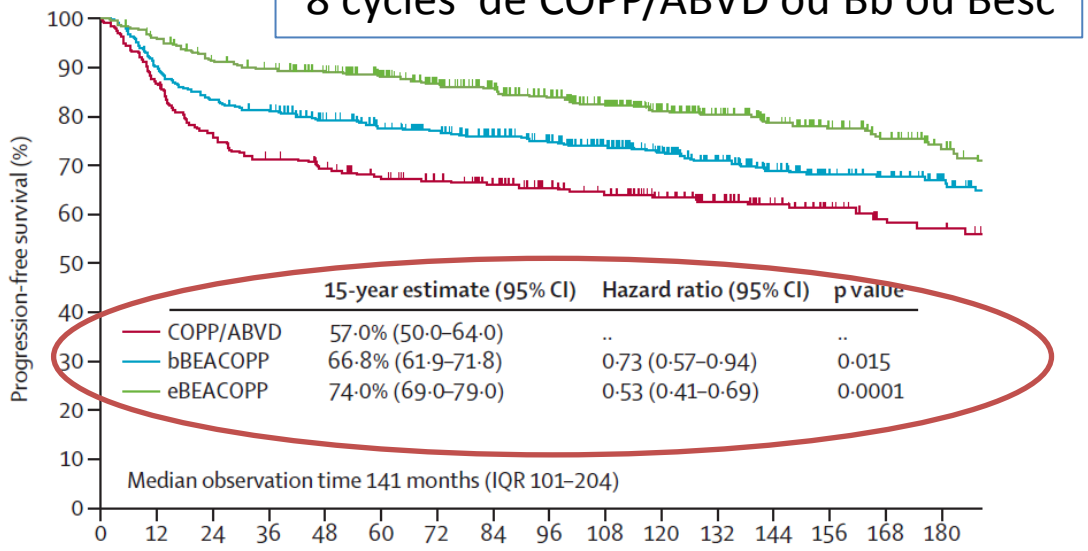
- Contrôle de la maladie insuffisant pour 25 à 30 % des pts

	n	CR	5y-PFS	Follow-up
Gordon JCO 2013	404	73%	74%	77 months
Chisesi JCO 2011	126	89%	78%	86 months
Viviani NEJM 2011	166	76%	73%	61 months
Federico JCO 2009	102	84%	68%	41 months
Hoskin JCO 2009	261	67%	76%	52 months

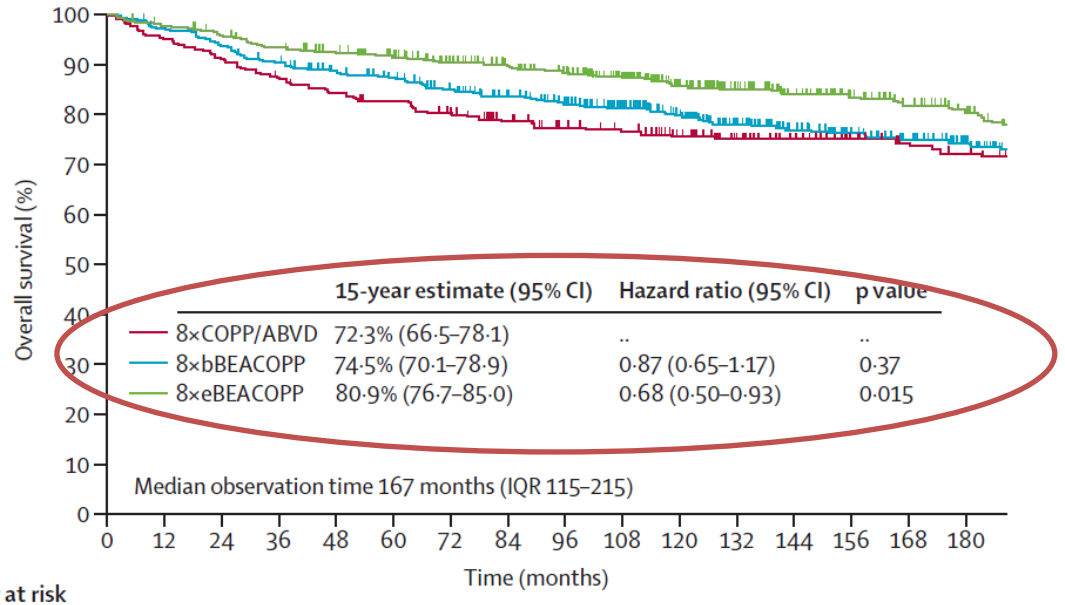
- Toxicité
  - Pulmonaire
    - Mayo clinic (n = 141): 18% des patients
    - MSKCC (n = 152): 22% d'arrêt précoce de la bleomycine
    - Hoskin et al (UK) : 10% de toxicité pulmonaire g>3
    - RATHL: Réduction de DLCO moyenne = 11% après 6 ABVD
      = 4.3% après 2 ABVD + 4 AVD

BEACOPP: HD9 à 15 ans

8 cycles de COPP/ABVD ou Bb ou Besc



Number at risk (number censored)				
COPP/ABVD	261 (0)	165 (12)	106 (62)	55 (106)
bBEACOPP	469 (0)	332 (33)	209 (138)	109 (225)
eBEACOPP	466 (0)	376 (36)	222 (164)	117 (255)

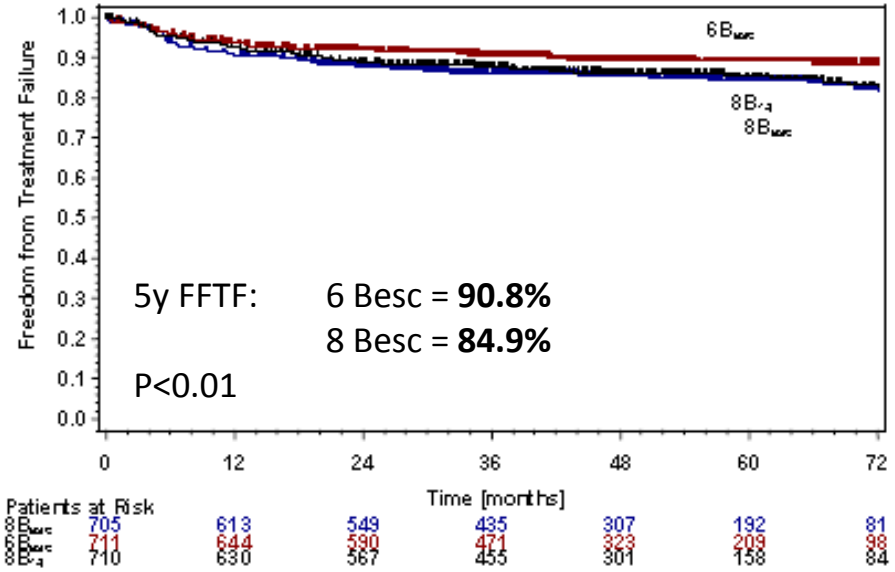


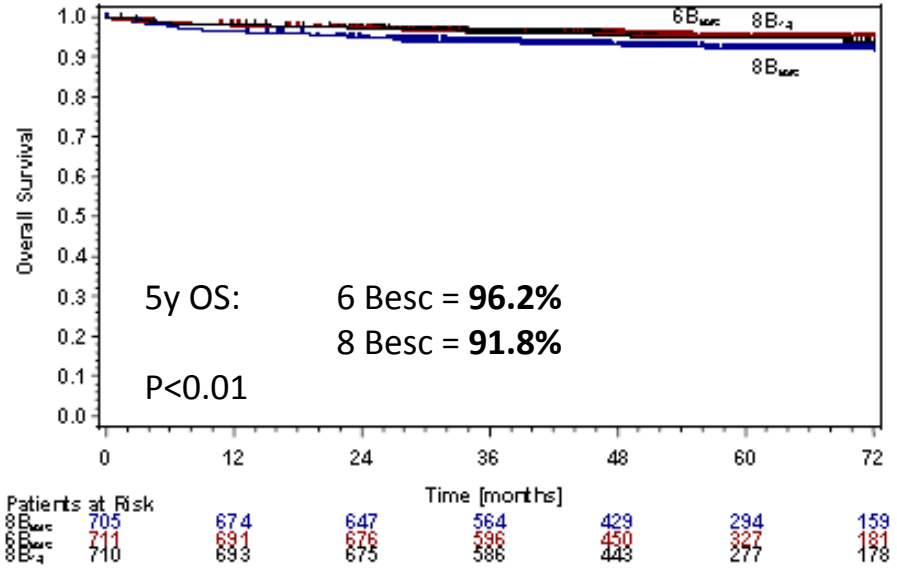
Number at risk (number censored)				
8×COPP/ABVD	261 (0)	212 (4)	157 (42)	99 (95)
8×bBEACOPP	469 (0)	389 (21)	271 (109)	159 (206)
8×eBEACOPP	466 (0)	406 (22)	275 (130)	166 (227)

	8 × COPP/ABVD plus RT (n=261)	8 × bBEACOPP plus RT (n=469)	8 × eBEACOPP plus RT (n=466)
Second primary malignant neoplasm*			
Acute leukaemia or MDS	1 (<1%)	8 (2%)†	15 (3%)
Non-Hodgkin lymphoma or myeloma	8 (3%)	12 (3%)	8 (2%)
Solid tumour	10 (4%)	28 (6%)	27 (6%)
Total	19 (7%)	48 (10%)	50 (11%)
10-year cumulative incidence (95% CI)	5·2% (2·4–8·0)	7·6% (5·0–10·2)	6·5% (4·1–8·9)
15-year cumulative incidence (95% CI)	7·2% (3·7–10·7)	13·0% (9·1–16·9)	11·4% (7·6–15·1)
Standardised incidence ratio (95% CI)	2·0 (1·2–3·2)	2·6 (1·9–3·4)	2·6 (1·9–3·4)

Von Treskow, Lancet Hematol 2018

BEACOPP: HD15





Causes of death - N (%)	BEACOPPesc x 8 (N=705)	BEACOPPesc x 6 (N=711)
Total	53 (7.5)	33 (4.6)
Hodgkin lymphoma	13 (1.8)	11 (1.5)
Toxicity of chemo	**15 (2.1)**	**6 (0.8)**
2nd Neoplasia	**13 (1.8)**	**5 (0.7)**
Toxicity of salvage treatment	2 (0.3)	2 (0.3)
Other	10 (1.4)	9 (1.3)

Engert A, Lancet 2012

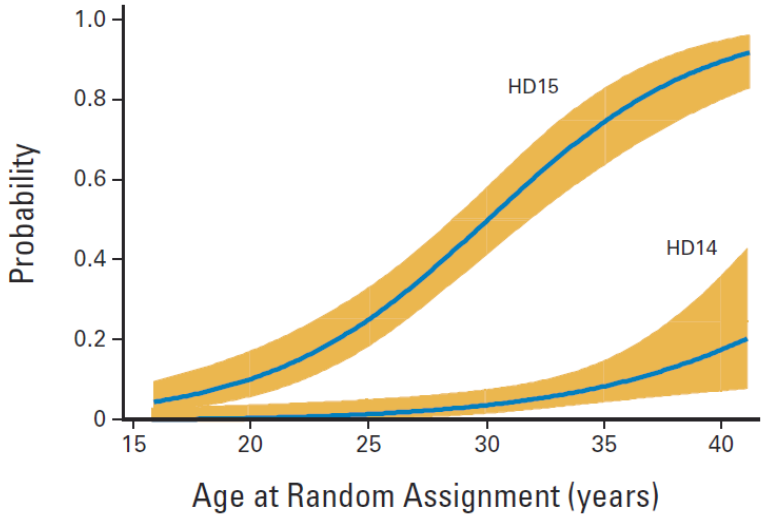
BEACOPPesc : Fertilité

- Hommes

  90% Azoospermie après 8 x BEACOPPesc

Sienawski, Ann Oncol, 2008

- Femmes: Aménorrhée 4 ans après fin Chimio



6-8 BEACOPPesc

4 BEACOPPesc + 4 BEACOPP

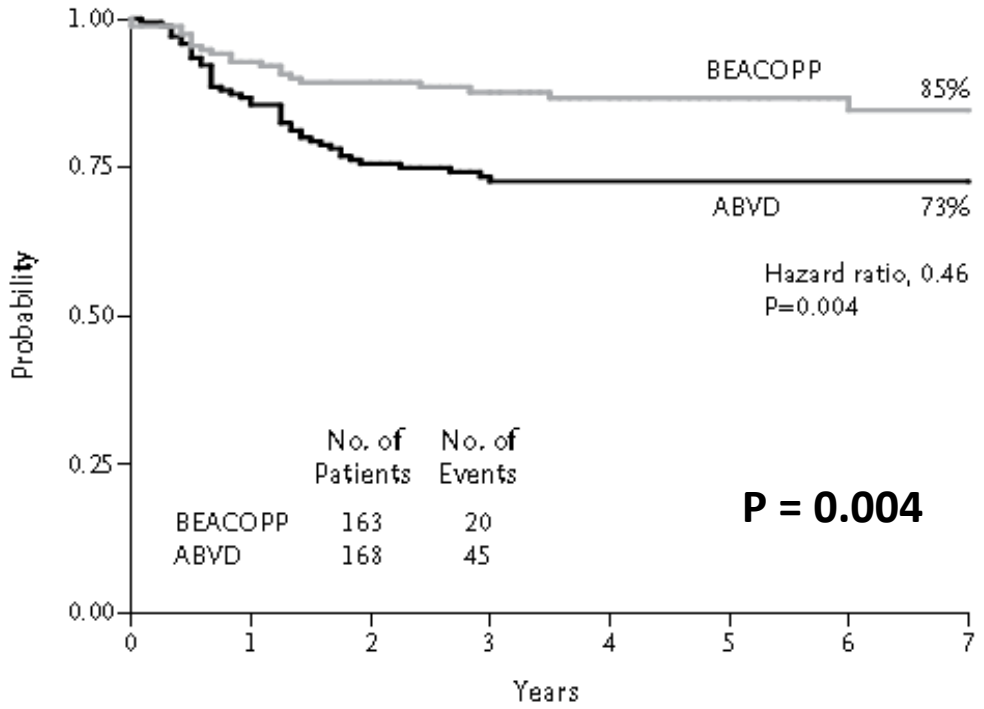
Behringer K, JCO, 2013

BEACOPP vs ABVD

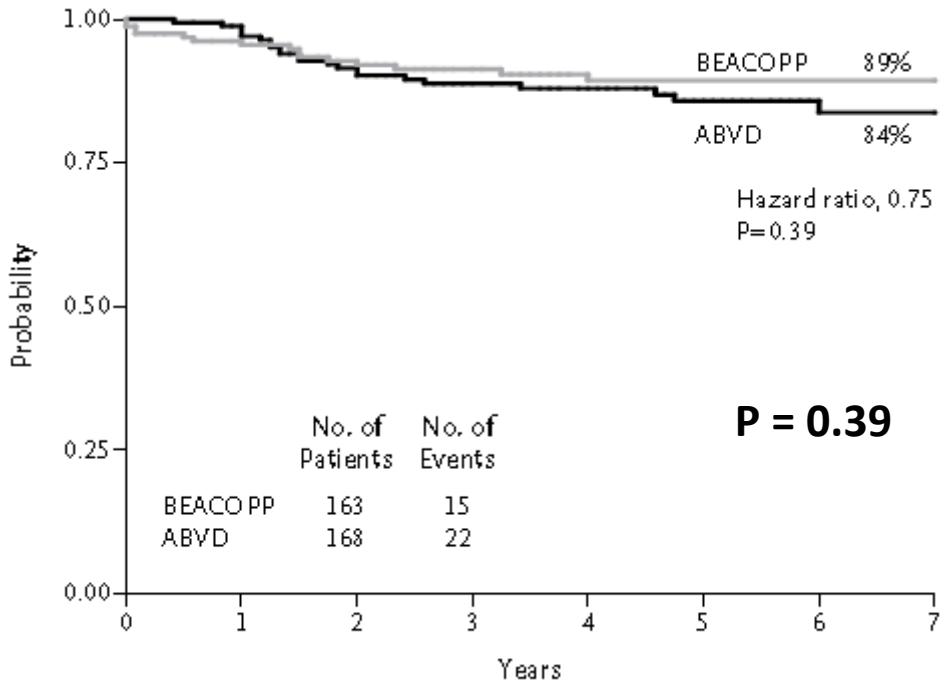
Stage IIB- IV
BEACOPP [esc x 4 + Baseline x 2 ou 4] vs ABVD

Median FU = 61 months

PFS



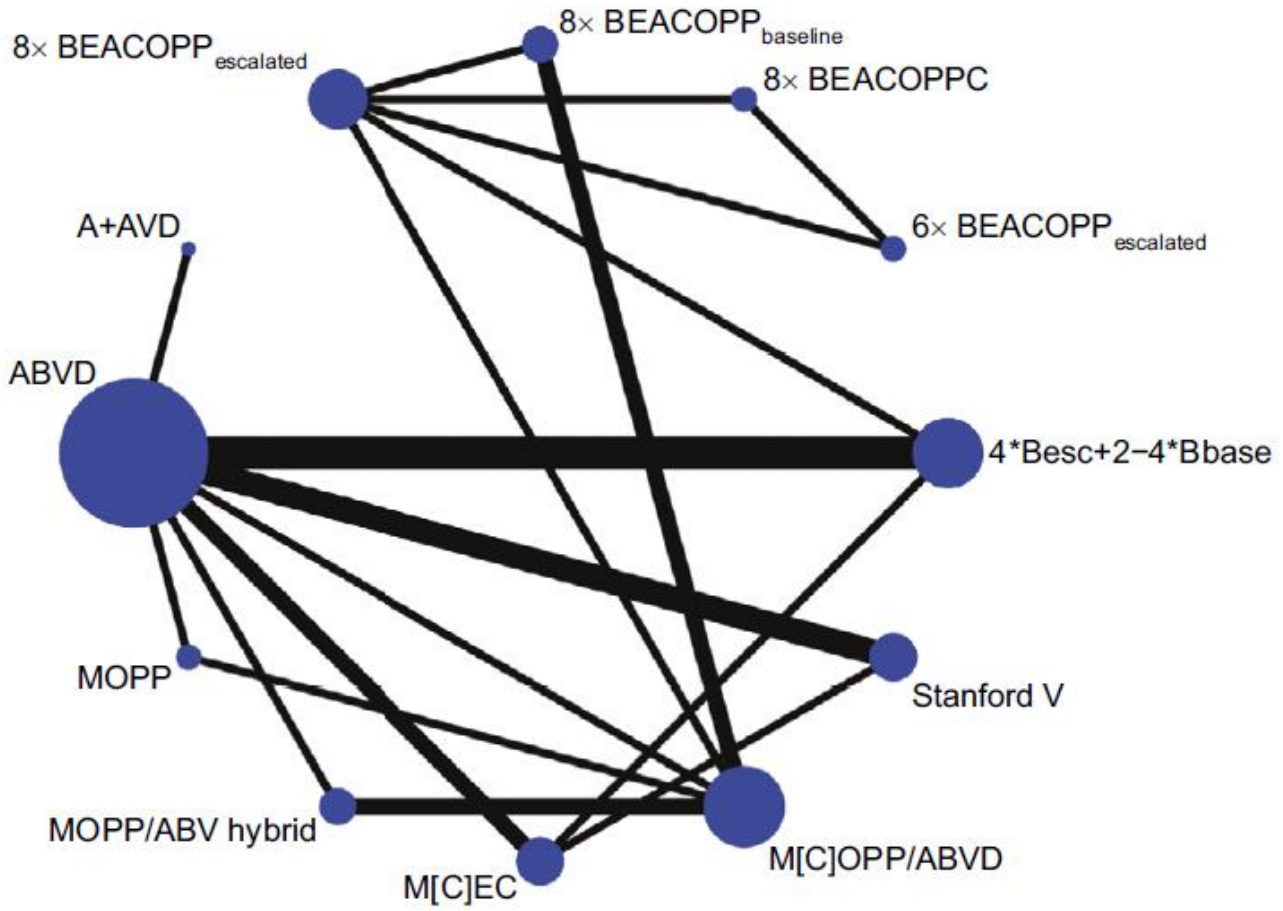
OS



Viviani S, NEJM 2011

BEACOPP vs ABVD

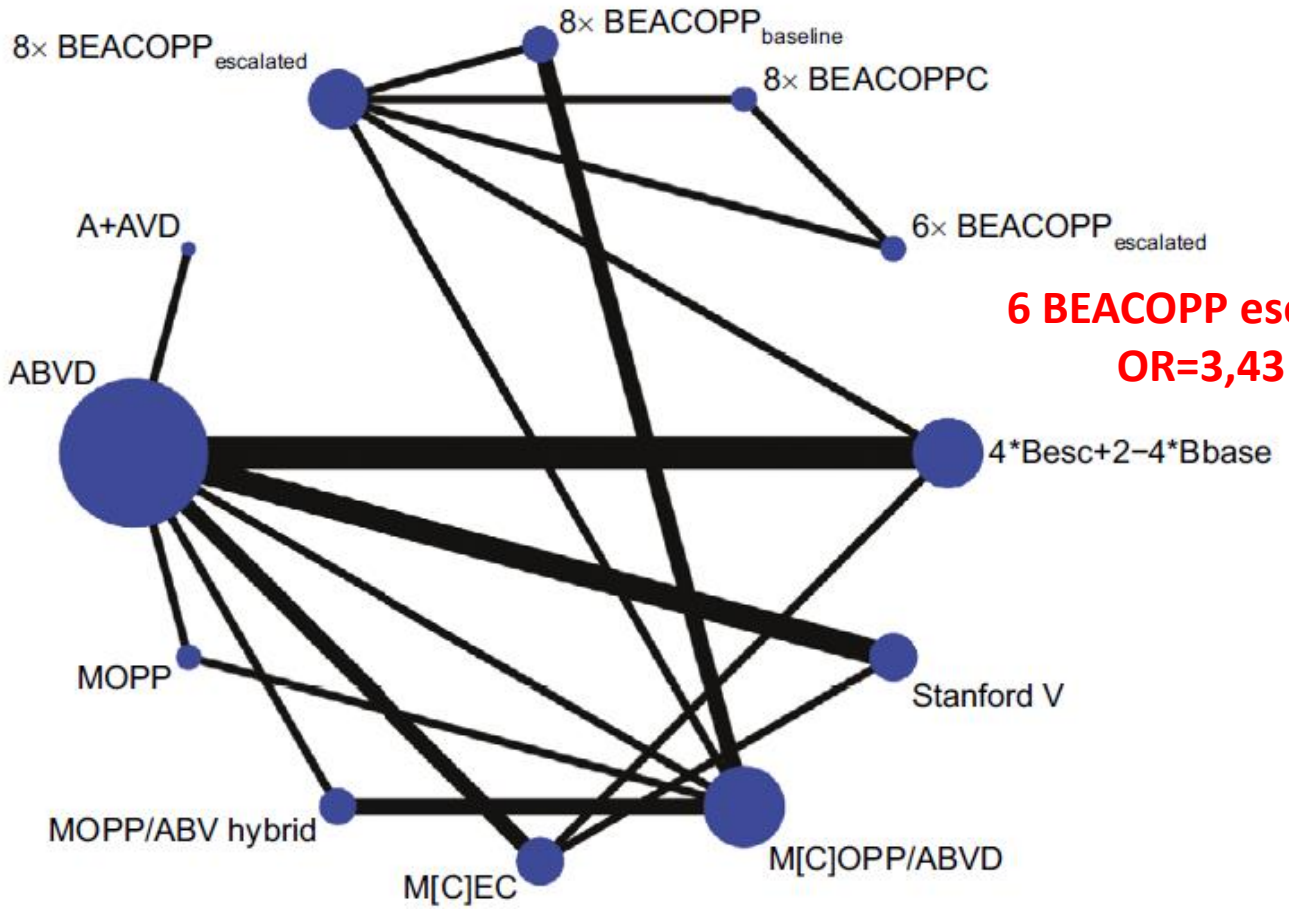
Représentation des comparaisons de différents schémas de traitement



Zhang et al., CMAR 2018

BEACOPP vs ABVD

Représentation des comparaisons de différents schémas de traitement



6 BEACOPP esc

OR=3,43 (IC95% 1,87-6,24)

Zhang et al., CMAR 2018

Les enjeux à l'ère de la TEP: formes avancées

- **ABVD guérit 70 à 75% des patients**

  => Améliorer le contrôle tumoral en identifiant les pts relevant d'un traitement plus intense?

- **BEACOPPesc guérit 85% des patients mais toxicités tardives**

  => Limiter la toxicité en maintenant le contrôle tumoral?

Les enjeux à l'ère de la TEP: formes avancées

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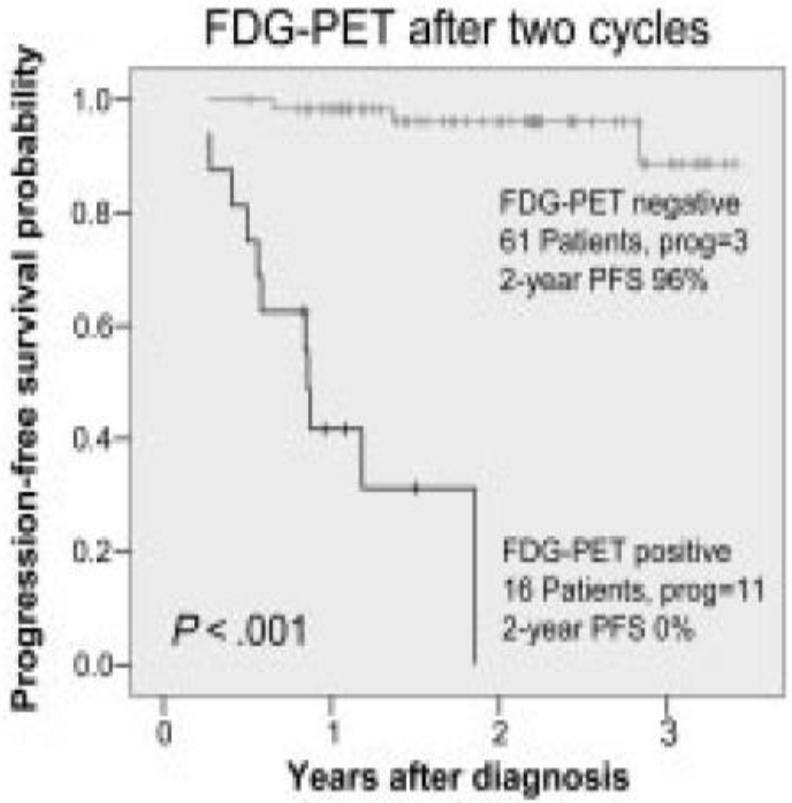
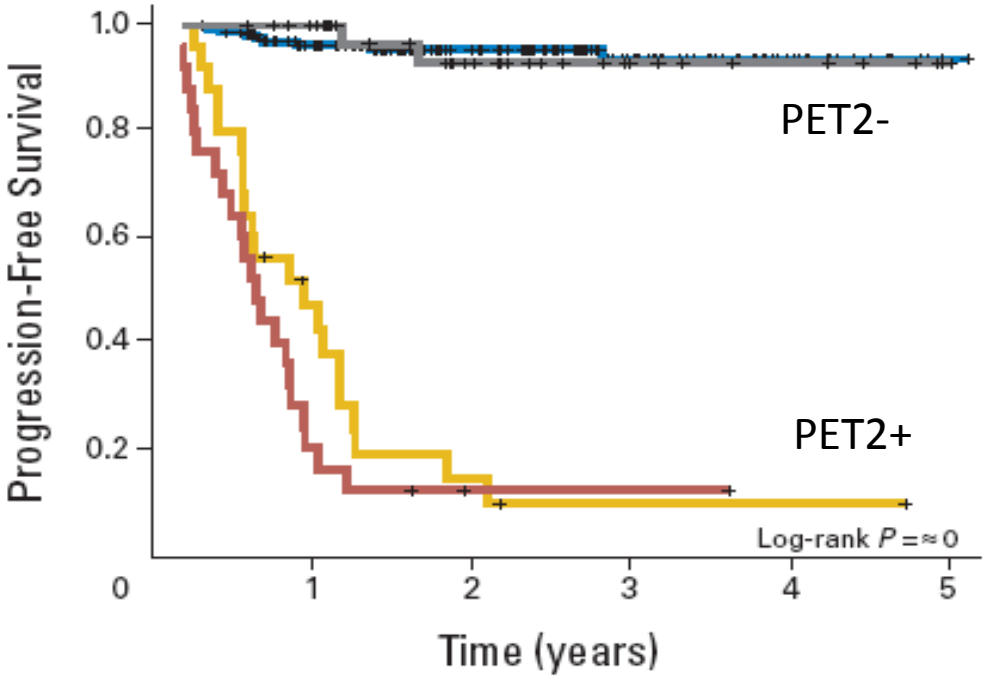
  => Limiter la toxicité en maintenant le contrôle tumoral?

Peut-on identifier les patients requérant du BEACOPPescaladé ?

La TEP précoce





Huchtings M, Blood 2006; 107: 52

Gallamini A, JCO 2007; 25: 3746

2 approches limitant l'exposition au BEACOPPesc

- **Réserver le BEACOPPesc aux mauvais répondeurs**

  Escalade des pts TEP2+ après ABVD

  – Inconvénients:
    - Dose intensité insuffisante pour les maladies les plus résistantes / sélection de clones résistants
    - VPP < VPN TEP2
  – Avantage: tolérance ABVD

- **Désescalade des pts TEP2- après BEACOPPesc pour tous**
  – Inconvénient: % TEP2- après BEACOPPesc?
  – Avantage: VPN > VPP TEP2

3 essais ABVD puis escalade des TEP2 pos

	Nb pts	PFS	OS	% TEP2 pos
RATHL (Johnson et al NEJM 2016)	1214	PFS à 3 ans: - des TEP 2 pos: 67,5% - des TEP 2 neg: 86%	OS à 3 ans: - des TEP 2 pos: 87,8% - des TEP 2 neg: 97%	16% (DS 4-5)
Press JCO 2016	336	PFS à 2 ans : - des TEP 2 pos: 64% - des TEP 2 neg: 82%	-	18% (DS=4-5)
HD 0607 (Gallamini et al JCO 2018)	1000	PFS à 2 ans : - des TEP 2 pos: 66% - des TEP 2 neg: 89%	-	19,6%

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Doctopic: Primary Research

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18TLO1387

Articles

Emilia

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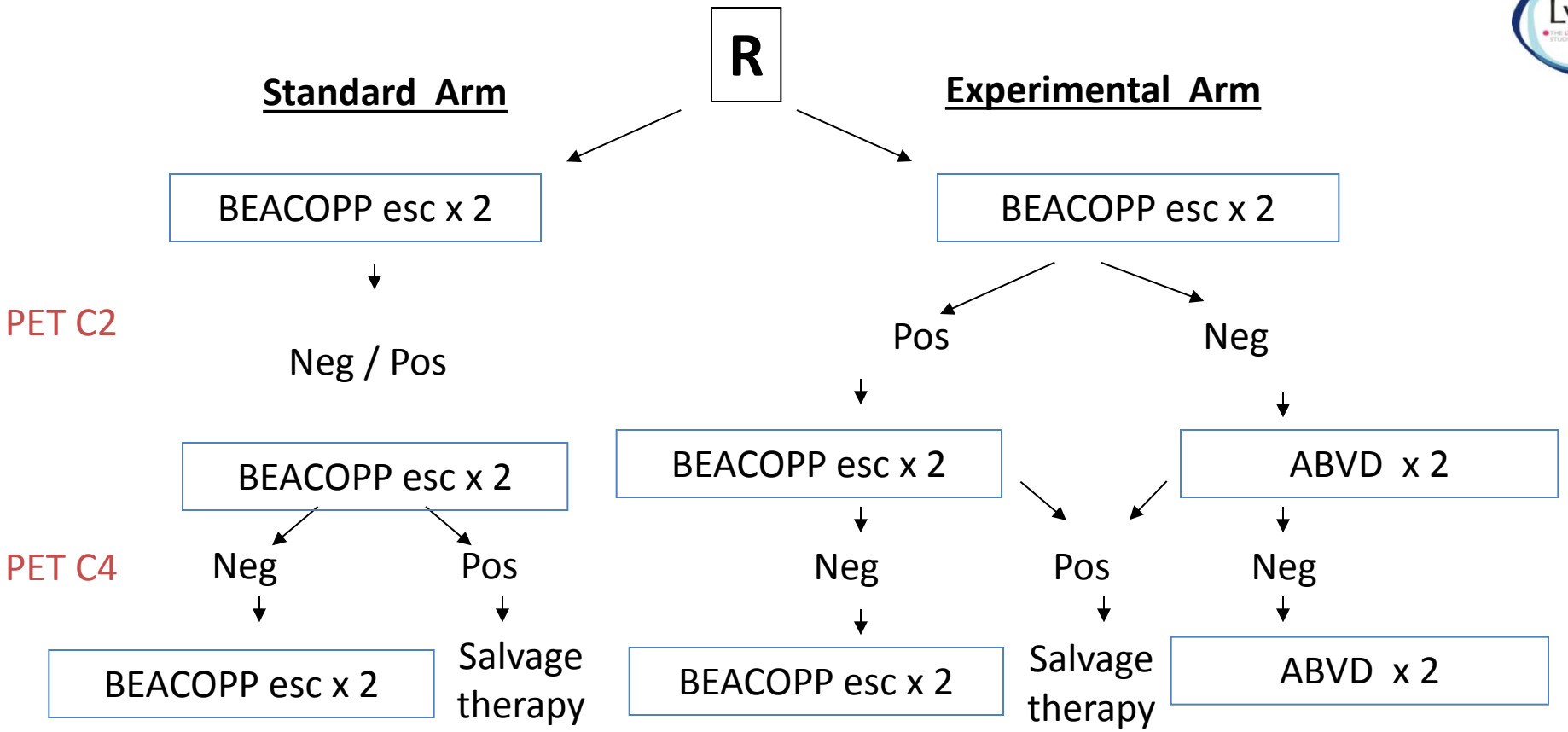
PET-adapted treatment for newly diagnosed advanced Hodgkin lymphoma (AHL2011): a randomised, multicentre, non-inferiority, phase 3 study

René-Olivier Casasnovas, Reda Bouabdallah, Pauline Brice, Julien Lazarovici, Hervé Ghesquieres, Aspasia Stamatoullas, Jehan Dupuis, Anne-Claire Gac, Thomas Gastinne, Bertrand Joly, Krimo Bouabdallah, Emmanuelle Nicolas-Virelizier, Pierre Feugier, Franck Morschhauser, Richard Delarue, Hassan Farhat, Philippe Quittet, Alina Berriolo-Riedinger, Adrian Tempescul, Véronique Edeline, Hervé Maisonneuve, Luc-Matthieu Fornecker, Thierry Lamy, Alain Delmer, Peggy Dartigues, Laurent Martin, Marc André, Nicolas Mounier, Alexandra Traverse-Glehen, Michel Meignan

AHL 2011



Casasnovas et al, Lancet Oncol 2019

AHL 2011: caractéristiques des patients

		Standard arm		Experimental arm		All	
		N = 413		N = 410		N = 823	
Median age (range)		31 (16 – 60)		29 (16-60)		30 (16 – 60)	
Male (n - %)		263	64%	253	62%	516	**63%**
ECOG (n - %)	0	203	49%	193	47%	396	48%
	1	177	44%	184	45%	361	45%
	2	27	7%	31	8%	58	7%
B symptoms (n - %)		282	68%	278	68%	560	**68%**
Ann Arbor stage (n - %)	I	0	0	2	0.5%	2	0.2%
	II	44	11%	52	13%	96	12%
	III	114	28%	115	28%	229	**28%**
	IV	255	62%	241	59%	496	**60%**
Stage IIB (n - %)		42	10%	45	13%	87	**11%**
	M/T≥ 0.33	41	98%	45	100%	86	99%
	Extra nodal localization	6	14%	4	9%	10	**12%**
Bone marrow involved (n - %)		33	8%	32	8%	65	8%
IPS group (n - %)	0-2	160	39%	183	45%	343	42%
	≥ 3	250	61%	225	55%	475	**58%**

Casasnovas et al, Lancet Oncol 2019

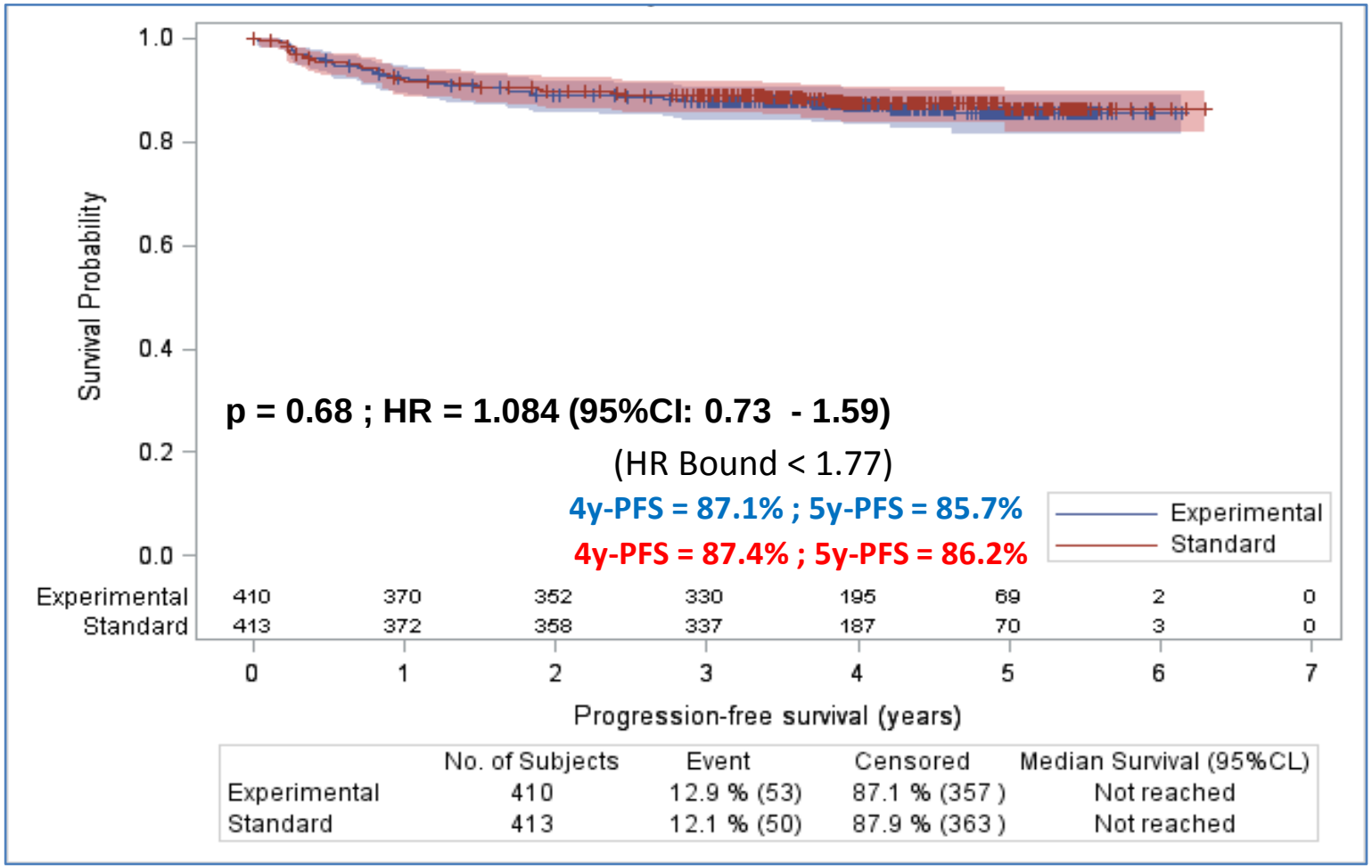
AHL 2011: résultats TEP 2 (central review)

	Standard arm n = 413		Experimental arm n = 410		All n = 823	
PET2						
Evaluable	398	96%	397	97%	795	97%
Negative	**349**	**88%**	**346**	**87%**	**695**	**87%**
Positive	**49**	**12%**	**51**	**13%**	**100**	**13%**

Casasnovas et al, Lancet Oncol 2019

AHL 2011: PFS selon le bras de traitement

(Primary endpoint – ITT population)



BEACOPP x 6

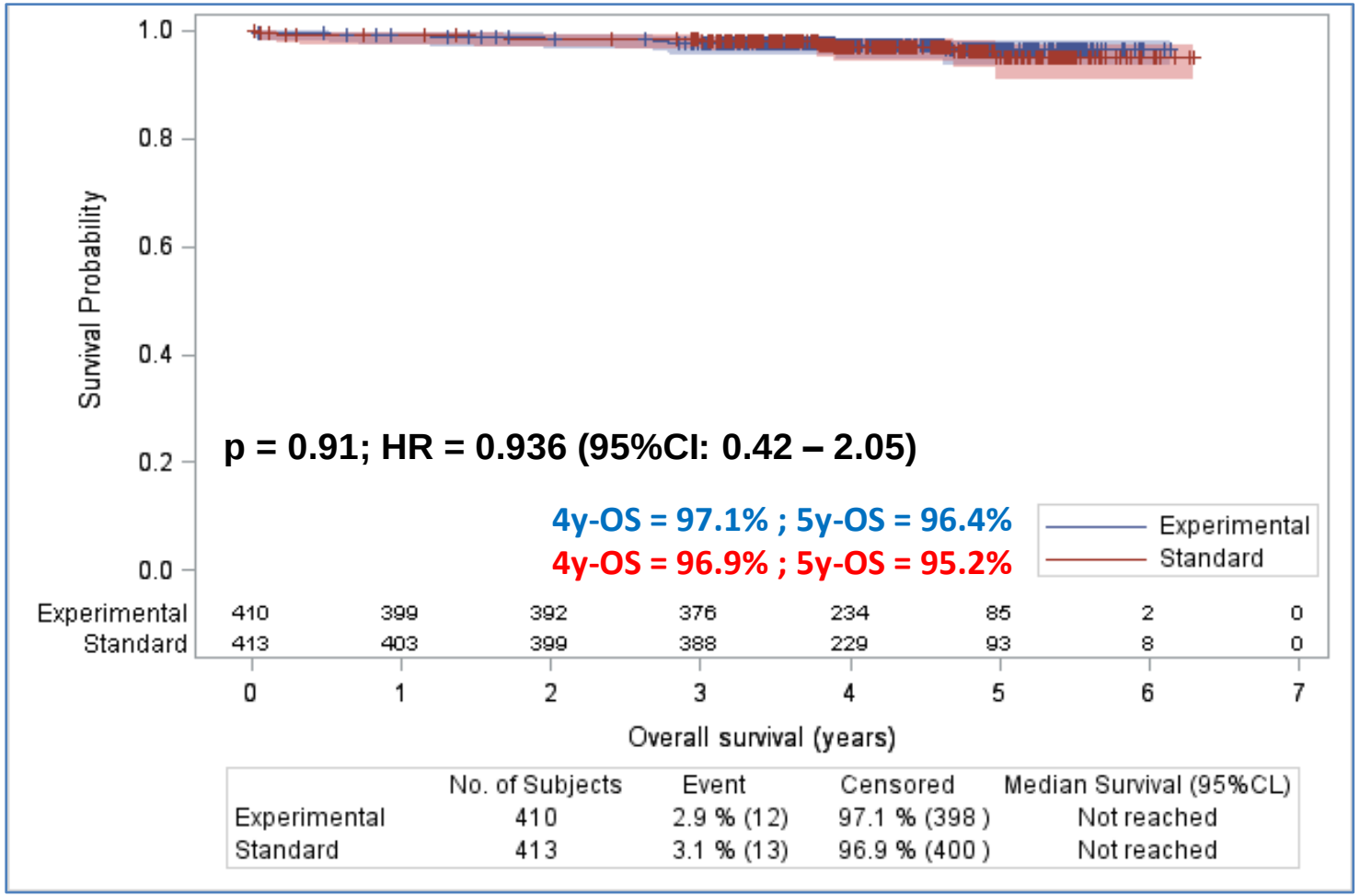
vs

BEACOPP x 6 (PET2+)
BEACOPP x 2 + ABVD x 4 (PET2-) (84%)

Median follow-up = 50.4 months

Casasnovas et al, Lancet Oncol 2019

AHL 2011: OS according to treatment arm



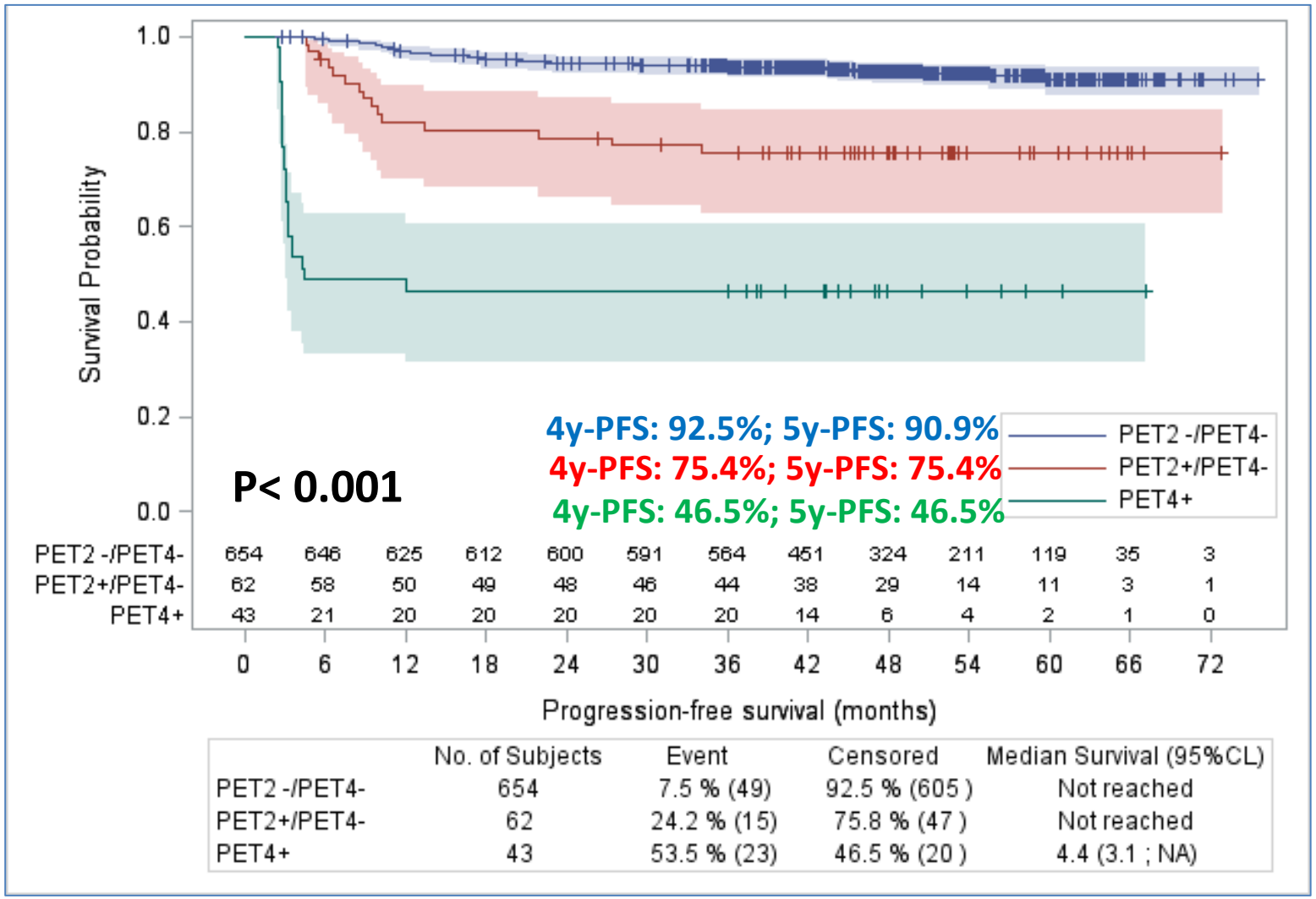
Casasnovas et al, Lancet Oncol 2019

AHL 2011: TEP 2 et 4 (central review)

	Standard arm n = 413		Experimental arm n = 410		All n = 823	
PET2						
Evaluable	398	96%	397	97%	795	97%
Negative	**349**	**88%**	**346**	**87%**	**695**	**87%**
Positive	**49**	**12%**	**51**	**13%**	**100**	**13%**
PET4						
Evaluable	383	93%	376	92%	759	92%
Negative	**356**	**93%**	**360**	**96%**	**716**	**94%**
Positive	**27**	**7%**	**16**	**4%**	**43**	**6%**

Casasnovas et al, Lancet Oncol 2019

AHL 2011: PFS selon la stratégie TEP-guidée



	No. of Subjects	Event	Censored	Median Survival (95%CL)
PET2 -/PET4-	654	7.5 % (49)	92.5 % (605)	Not reached
PET2+/PET4-	62	24.2 % (15)	75.8 % (47)	Not reached
PET4+	43	53.5 % (23)	46.5 % (20)	4.4 (3.1 ; NA)

n = 654 (86%)

n = 64 (8%)

n = 43 (6%)

Casasnovas et al, Lancet Oncol 2019

AHL 2011: Facteurs influençant la PFS

Risk factors		n (%)	4y-PFS % (95%CI)	Univariate analysis HR	Univariate analysis p	Multivariate analysis HR	Multivariate analysis p
PET2/PET4	PET2-/PET4-	654 (79%)	92.5 (90.1-94.3)				
	PET2+/PET4-	62 (7.5%)	75.4 (62.5-84.4)	**3.588**	**<0.0001**	**3.316**	**<0.0001**
	PET4+	43 (5.2%)	46.5 (31.2-60.4)	**13.14**	**<0.0001**	**12.968**	**<0.0001**
IPS	0-2	343 (42%)	91.9 (88.4-94.4)				
	≥3	475 (58%)	83.7 (79.9-86.9)	**1.915**	**0.0025**	**1.6**	**0.044**

Casasnovas et al, Lancet Oncol 2019

AHL 2011: Effets indésirables

	Standard Arm n = 412		PET-driven arm n = 407		
	n	%	n	%	p
Patients with AE of any grade	412	100	407	100	NS
Patients with AE Grade ≥3	402	98	394	97	NS
AE grade ≥3					
Blood and lymphatic system disorders	400	97	388	95	NS
Anemia	286	69	114	28	**<0.001**
Leukopenia	381	92	367	9	NS
Neutropenia	359	87	366	9	NS
Febrile neutropenia	145	35	93	23	**<0.001**
Thrombocytopenia	271	66	163	40	**<0.001**
Infections and infestations	78	19	43	11	**<0.001**
Sepsis	29	7	15	4	**0.04**
Lung infection	12	3	4	1	NS
Other	48	12	28	7	**0.02**
Gastro-intestinal disorders	41	10	41	10	NS

Casasnovas et al, Lancet Oncol 2019

AHL 2011: Impact sur la Fertilité

- A dedicated study is ongoing ,testing:
  - Female:
    - AMH, inhibin B, 17-beta-oestradiol, FSH, LH levels
  - Male
    - Spermogram
    - FSH, testosterone
  - All:
    - Fertility history including spontaneous pregancy, medical assisted procreation
    - Fertility preservation procedure
- To date:
  - 73 Pregnancies : **n=28 (6.8%) in Standard and 45 (11%) in the PET-driven arms (p = 0.036)**
  - Medical assisted procreation : 6 (21%) vs 6 (7%) in Standard and PET-driven arms respectively

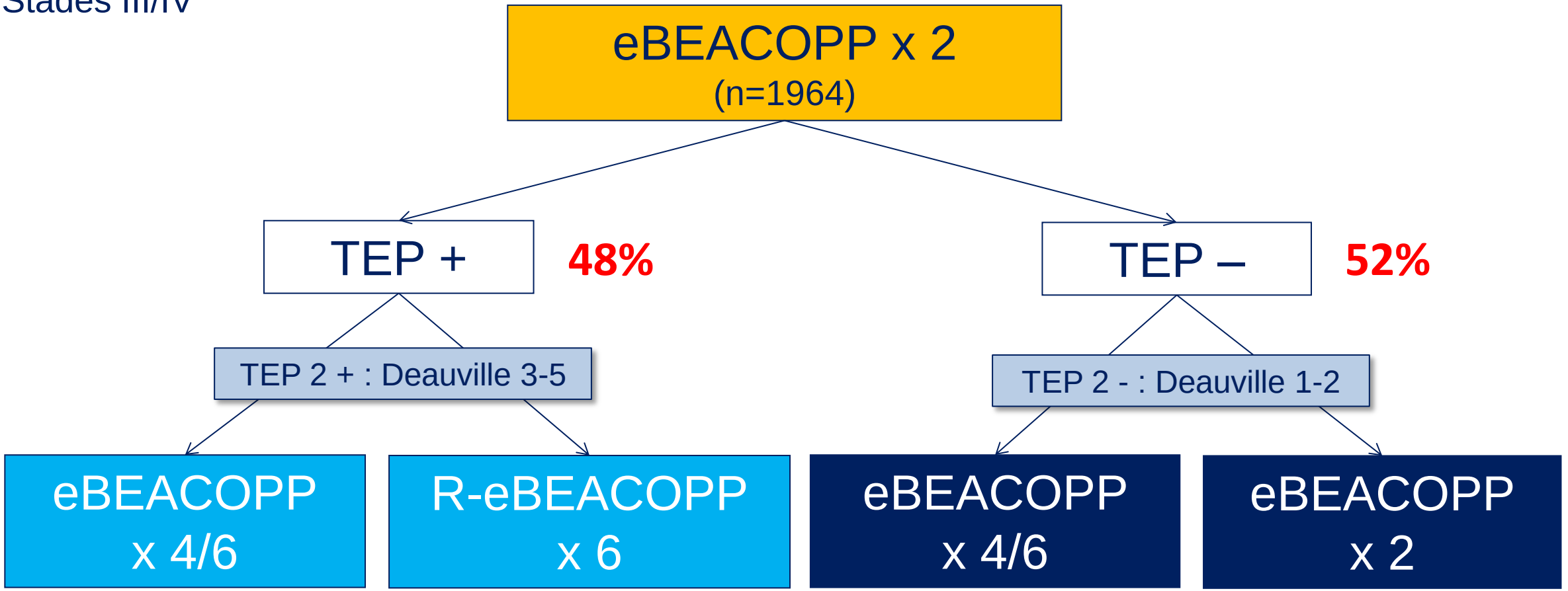
Casasnovas et al, Lancet Oncol 2019

Autres approches

- Réduire le nombre de cycles de BEACOPP : **HD18**
- Escalade thérapeutique si TEP2 positive après ABVD : **RATHL**
- Incorporer les nouvelles drogues dès la 1ère ligne :
  - **Brentuximab vedotin : BrECADD & Echelon 1**
  - **Nivolumab : Checkmate 205 (Cohorte D)**

Essai HD18

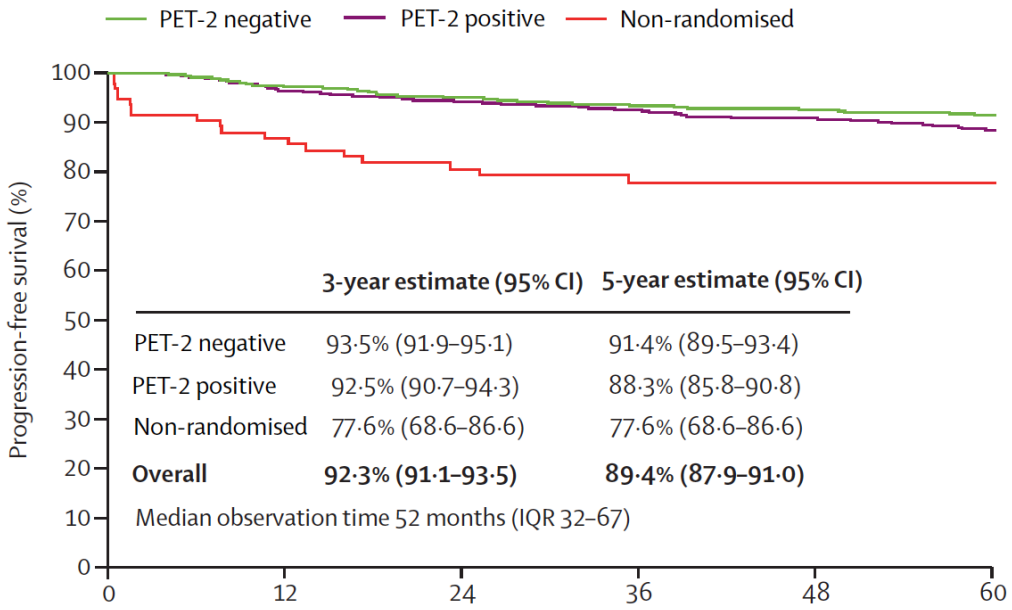
Stades IIB avec FR (bulk, extranodal)
Stades III/IV



Borchmann P, Lancet 2017

Essai HD18

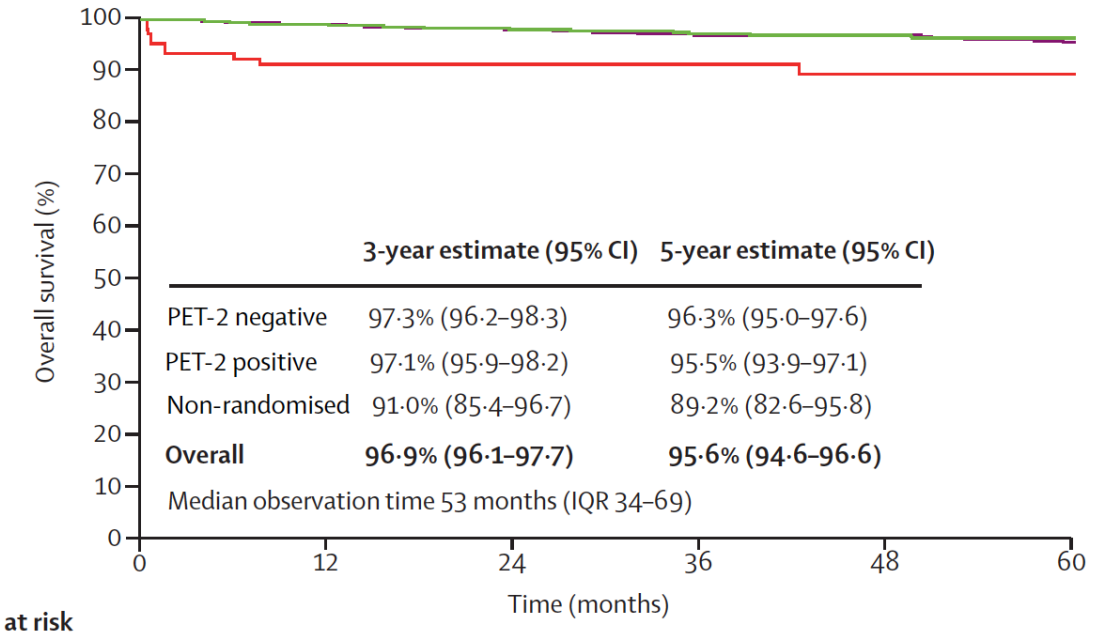
Rôle pronostique de la TEP 2 : **DS 1-2 vs 3-5**



	3-year estimate (95% CI)	5-year estimate (95% CI)
PET-2 negative	93·5% (91·9–95·1)	91·4% (89·5–93·4)
PET-2 positive	92·5% (90·7–94·3)	88·3% (85·8–90·8)
Non-randomised	77·6% (68·6–86·6)	77·6% (68·6–86·6)
Overall	**92·3% (91·1–93·5)**	**89·4% (87·9–91·0)**

Median observation time 52 months (IQR 32–67)

Number at risk (number censored)						
PET-2 negative	1010 (0)	921 (63)	845 (118)	685 (265)	548 (396)	385 (553)
PET-2 positive	948 (0)	854 (62)	766 (131)	600 (284)	476 (398)	276 (588)
Non-randomised	115 (0)	72 (31)	61 (37)	47 (49)	35 (61)	24 (72)



	3-year estimate (95% CI)	5-year estimate (95% CI)
PET-2 negative	97·3% (96·2–98·3)	96·3% (95·0–97·6)
PET-2 positive	97·1% (95·9–98·2)	95·5% (93·9–97·1)
Non-randomised	91·0% (85·4–96·7)	89·2% (82·6–95·8)
Overall	**96·9% (96·1–97·7)**	**95·6% (94·6–96·6)**

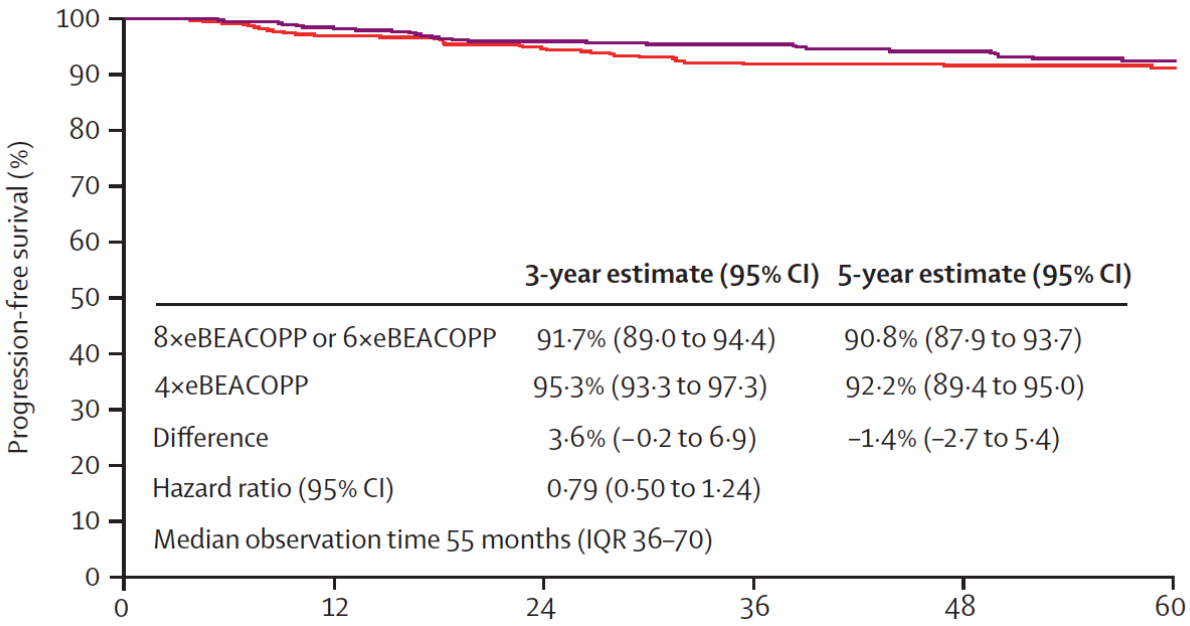
Median observation time 53 months (IQR 34–69)

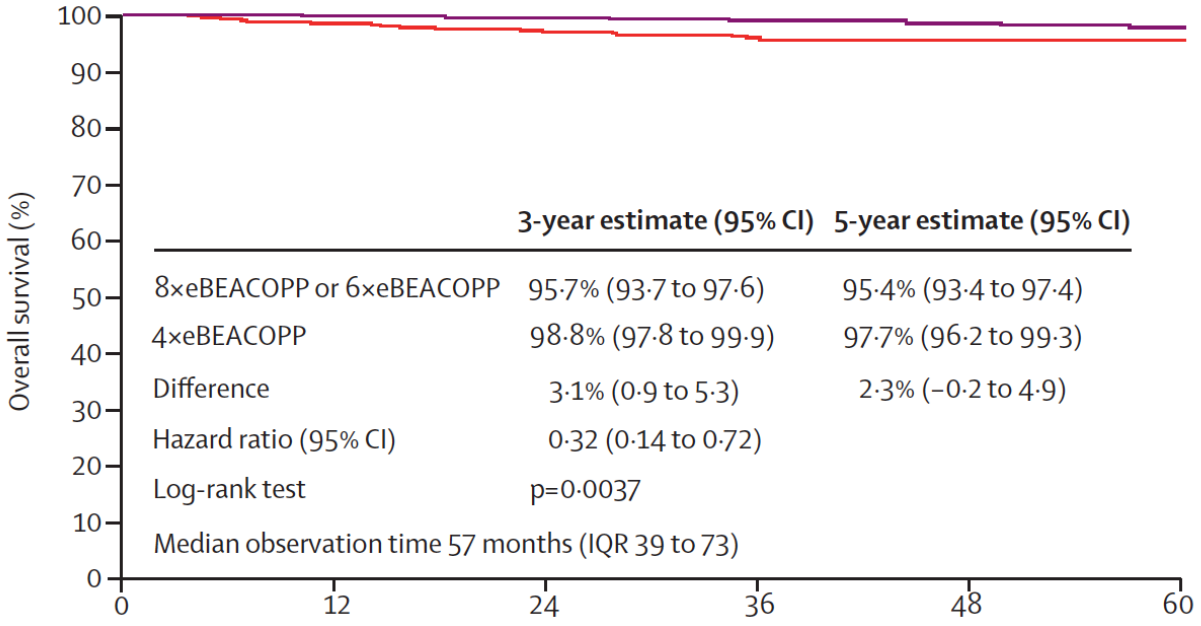
Number at risk (number censored)						
PET-2 negative	1010 (0)	960 (41)	902 (90)	737 (248)	594 (388)	437 (542)
PET-2 positive	948 (0)	902 (37)	824 (107)	641 (282)	521 (401)	325 (591)
Non-randomised	115 (0)	76 (30)	67 (39)	54 (52)	40 (65)	26 (79)

Borchmann P, Lancet 2017

Essai HD18

Patients TEP 2 négative **(DS 1-2)**





Borchmann P, Lancet 2017

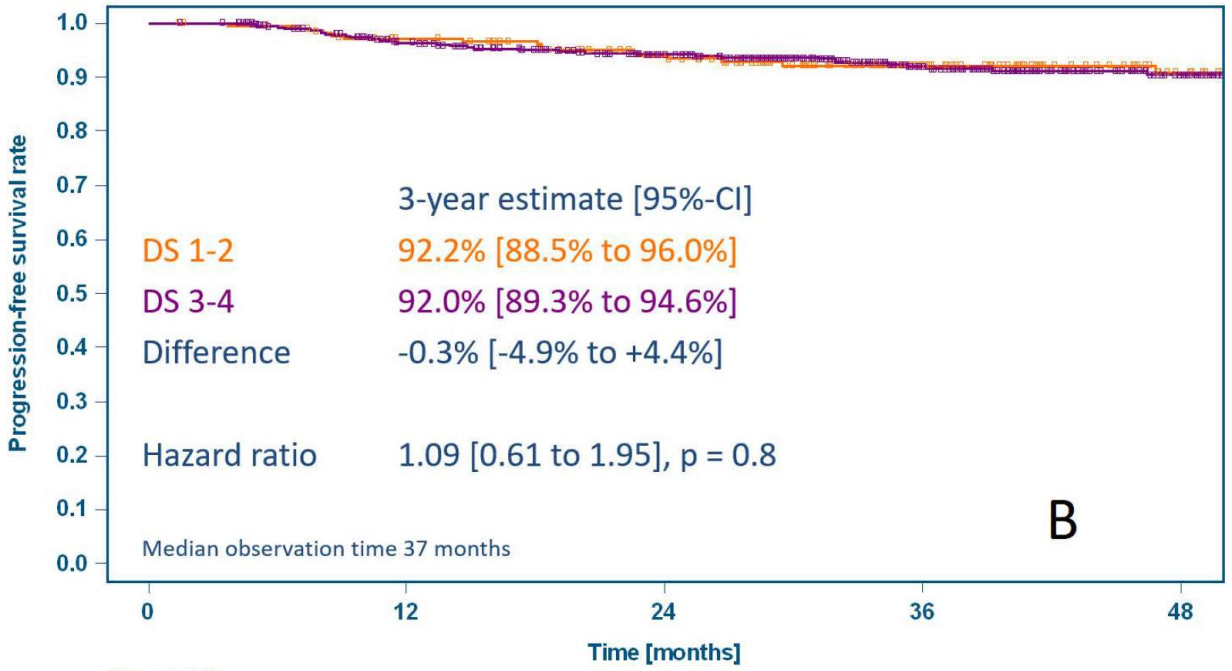
Essai HD18

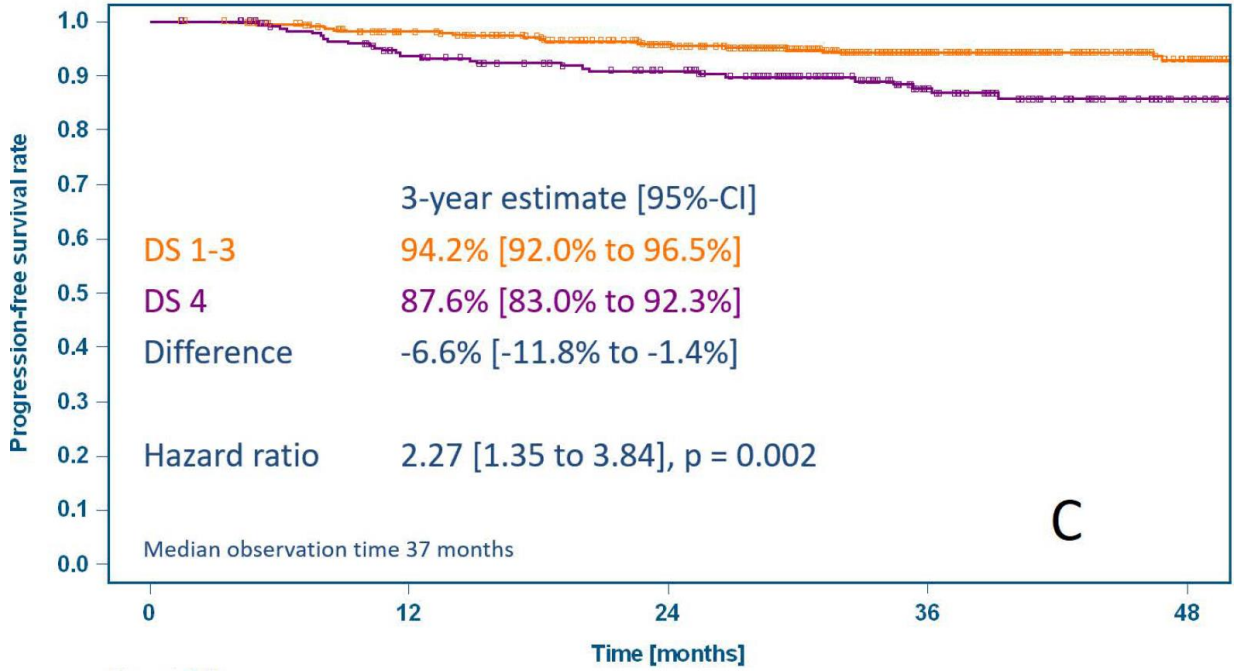
	PET-2-positive cohort		PET-2-negative cohort	
	8 × eBEACOPP (n=217)	8 × R-eBEACOPP (n=217)	8 × eBEACOPP or 6 × eBEACOPP (n=504)	4 × eBEACOPP (n=501)
Causes of death				
Hodgkin's lymphoma	1 (<1%)	1 (<1%)	3 (1%)	4 (1%)
Toxicity of study treatment	1 (<1%)	3 (1%)	6 (1%)	0
Toxicity of salvage therapy	3 (1%)	4 (2%)	2 (<1%)	2 (<1%)
Second malignancy	2 (1%)	2 (1%)	11 (2%)	1 (<1%)
Other disease*	2 (1%)	2 (1%)	1 (<1%)	1 (<1%)
Accident or suicide	0	2 (1%)	0	1 (<1%)
Unclear	0	0	2 (<1%)	0
Any event	9 (4%)	14 (6%)	25 (5%)	9 (2%)
Second malignancies				
Acute myeloid leukaemia or myelodysplastic syndrome	5 (2%)	4 (2%)	8 (2%)	2 (<1%)
Non-Hodgkin's lymphoma	3 (1%)	2 (1%)	5 (1%)	8 (2%)
Solid tumour	2 (1%)	8 (4%)	5 (1%)	3 (1%)
Any event	10 (5%)	8 (4%)	18 (4%)	13 (3%)
5-year cumulative incidence estimate†	4·0% (1·3–6·7)	3·5% (0·7–6·3)	3·8% (1·9–5·7)	3·3% (1·4–5·3)

Borchmann P, Lancet 2017

Essai HD18

Rôle pronostique de la TEP 2 : **DS 1-3 vs 4**

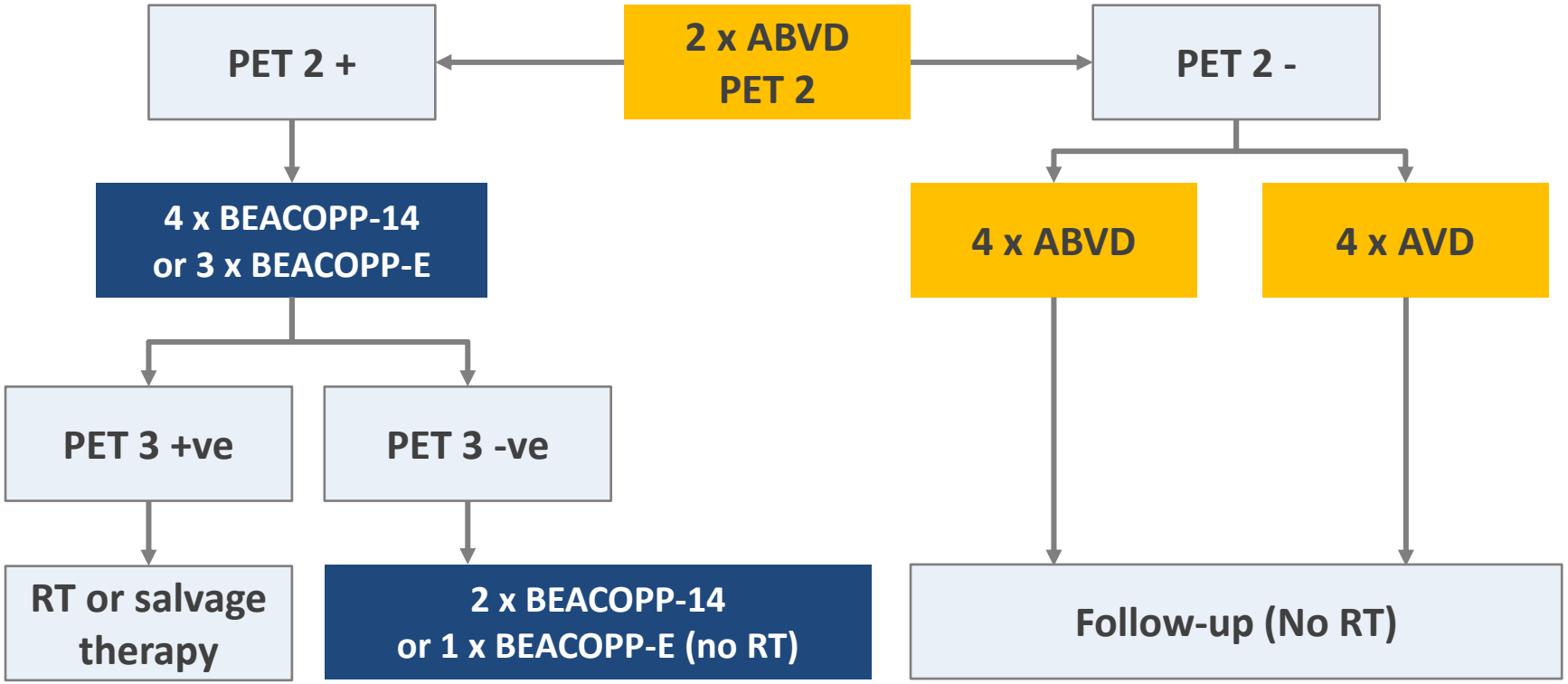




Patients traités par 6 cycles de eBEACOPP

Kobe C, Blood 2018

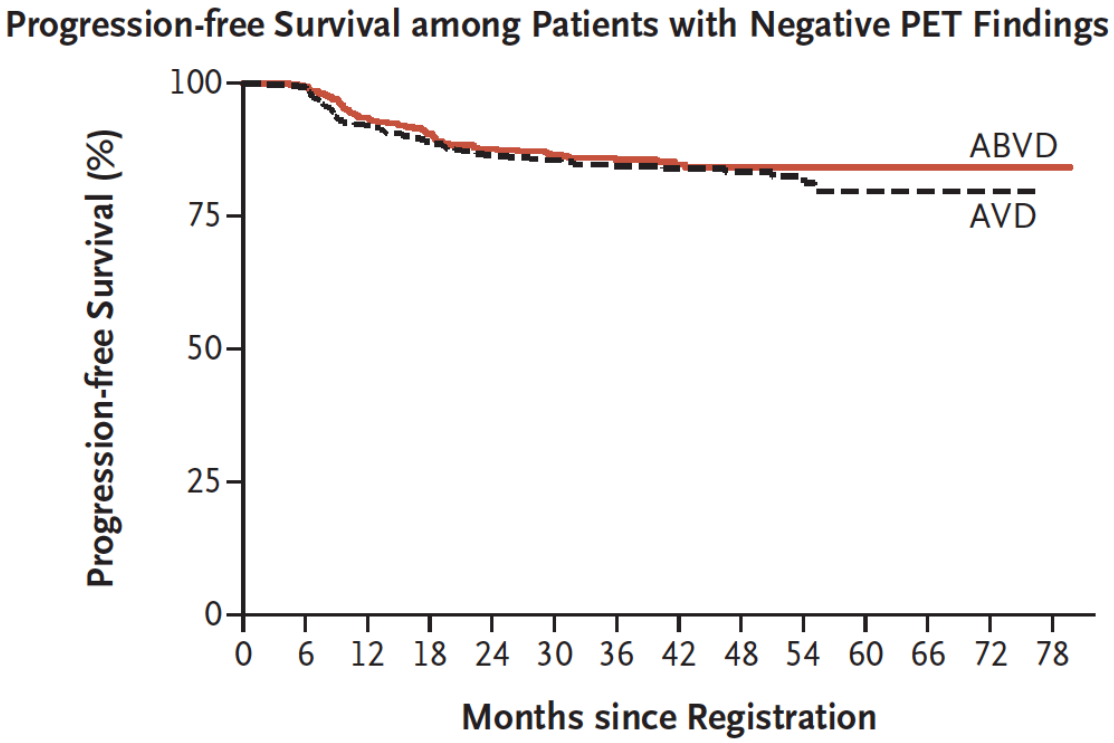
Essai RATHL

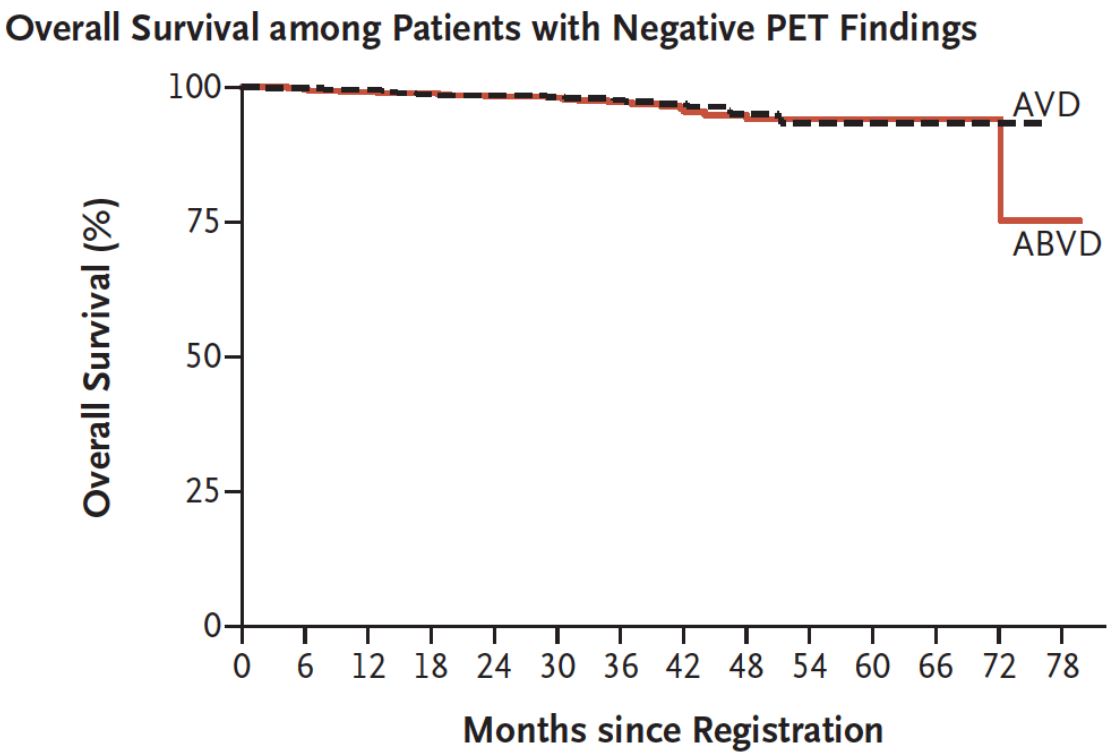


- Stades II / III / IV : 41% / 31% / 28%
- IPS > 3 : 17%

Johnson P, NEJM 2016

Essai RATHL





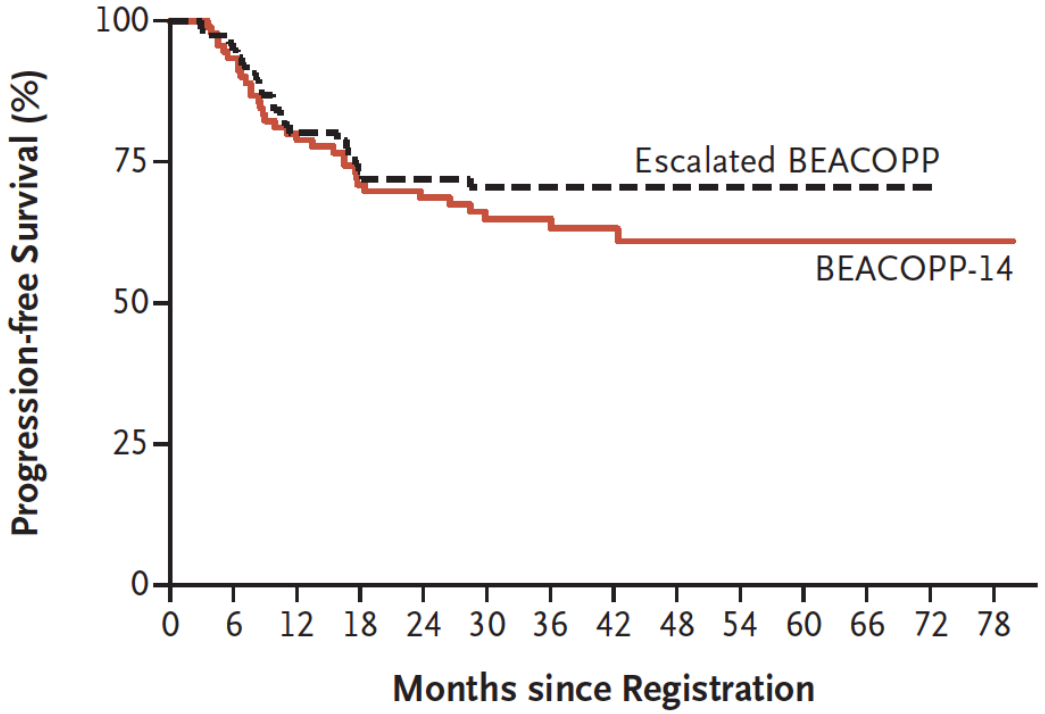
3y-PFS : 85.7% vs 84.4%

HR=1.13, 95% CI 0.81-1.57, p=0.48

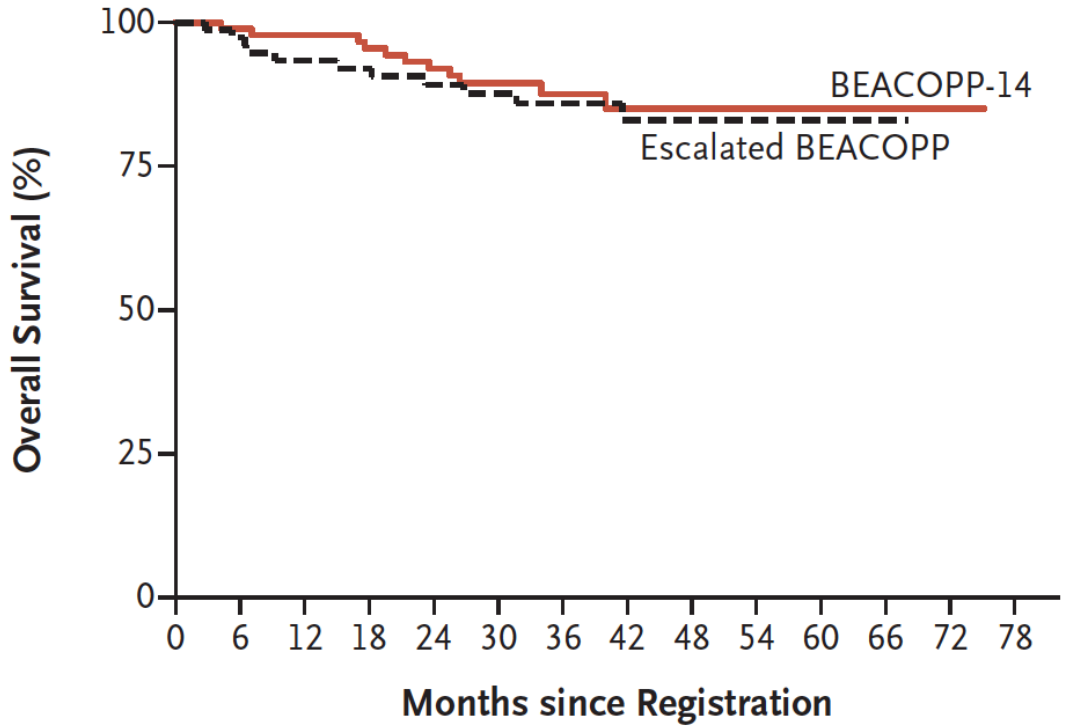
Johnson P, NEJM 2016

Essai RATHL

Progression-free Survival among Patients with Positive PET Findings



Overall Survival among Patients with Positive PET Findings



3y-PFS : 67.5%
3y-OS : 87.8%

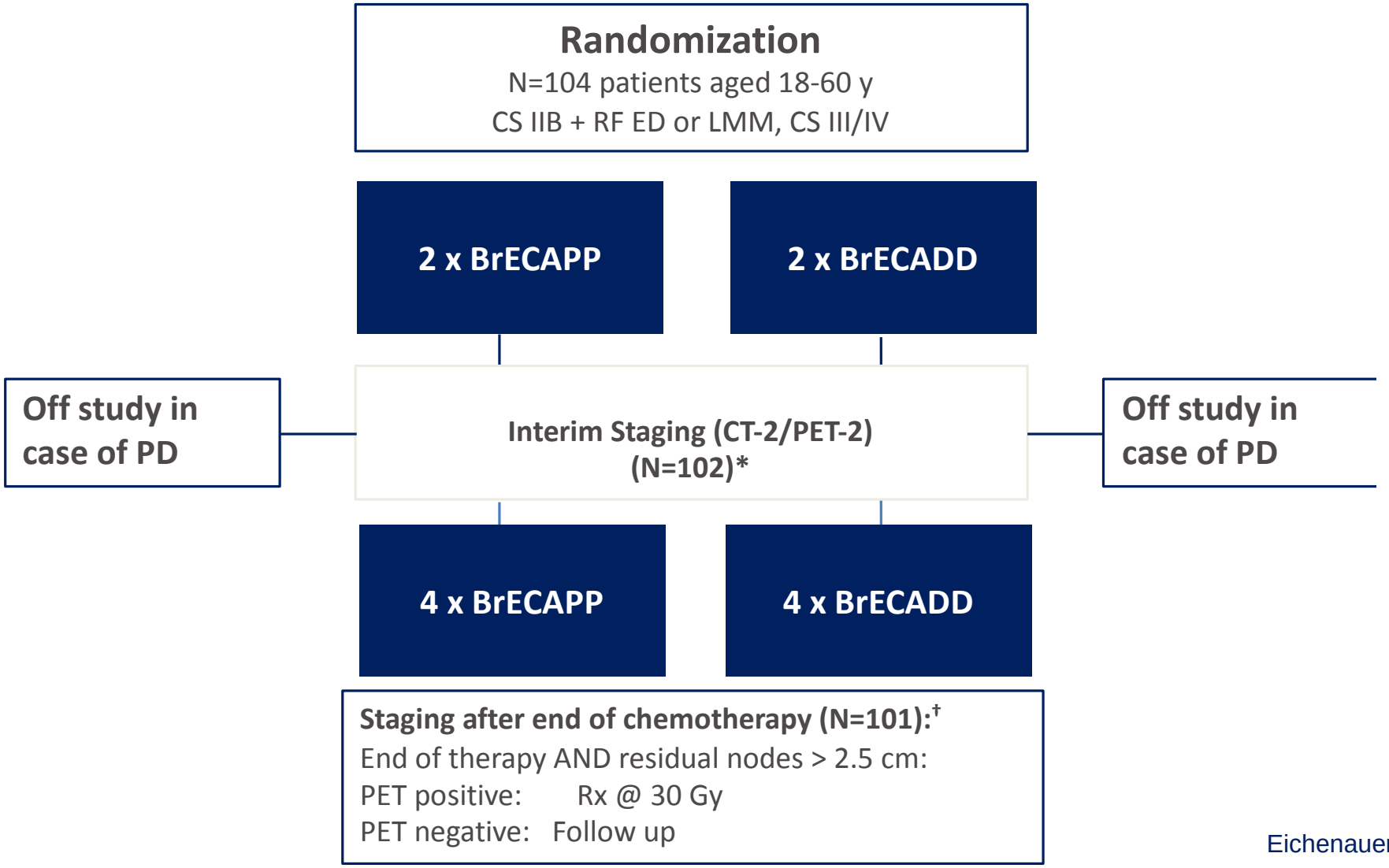
Johnson P, NEJM 2016

Schémas BrECADD/BrECAPP

Drug	Day	eBEACOPP	BrECADD	BrECAPP
Bleomycin (mg/m²)	8	10	–	–
Etoposide (mg/m²)	1–3	200	150	200
Doxorubicin (mg/m²)	1	35	**40**	35
Cyclophosphamide (mg/m²)	1	1250	1250	1250
Vincristine (mg/m²)	8	1.4	–	–
Brentuximab vedotin (mg/kg)	**1**	–	**1.8**	**1.8**
Procarbazine (mg/m²)	1–7	100	–	100
Dacarbazine (mg/m²)	**2–3**	–	**250**	–
Prednisone (mg)	1–14	40	–	40
Dexamethasone (mg)	**1–4**	–	**40**	–

Eichenauer D, Lancet Oncol 2017

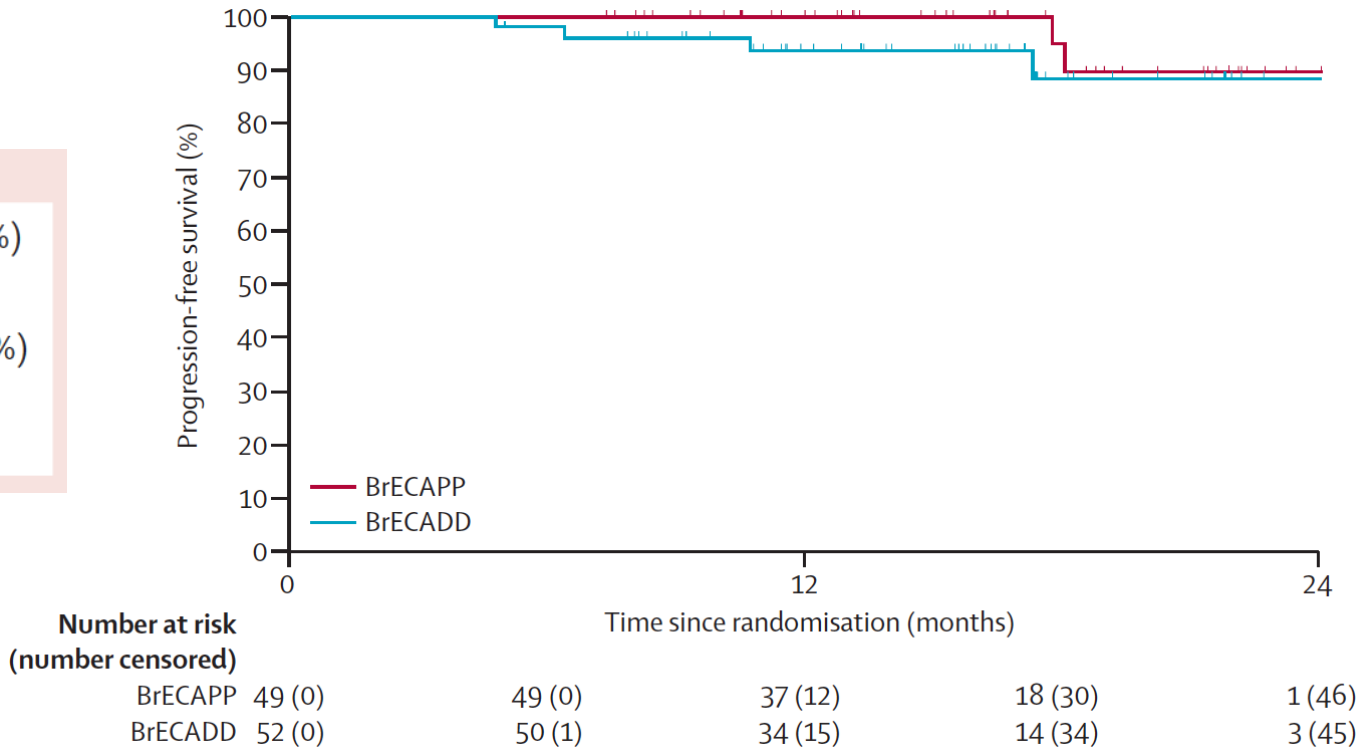
Schémas BrECADD/BrECAPP



Eichenauer D, Lancet Oncol 2017

Schémas BrECADD/BrECAPP

	BrECAPP	BrECADD
Complete response to chemotherapy		
No (further treatment recommended by CREP)	7/49 (14%)	6/52 (12%)
Yes (CR or PR <2·5 cm [local investigator] or no indication for further treatment [CREP])	42/49 (86%)	46/52 (88%)



18mo-PFS : 95% (BrECAPP) & 89% (BrECADD)

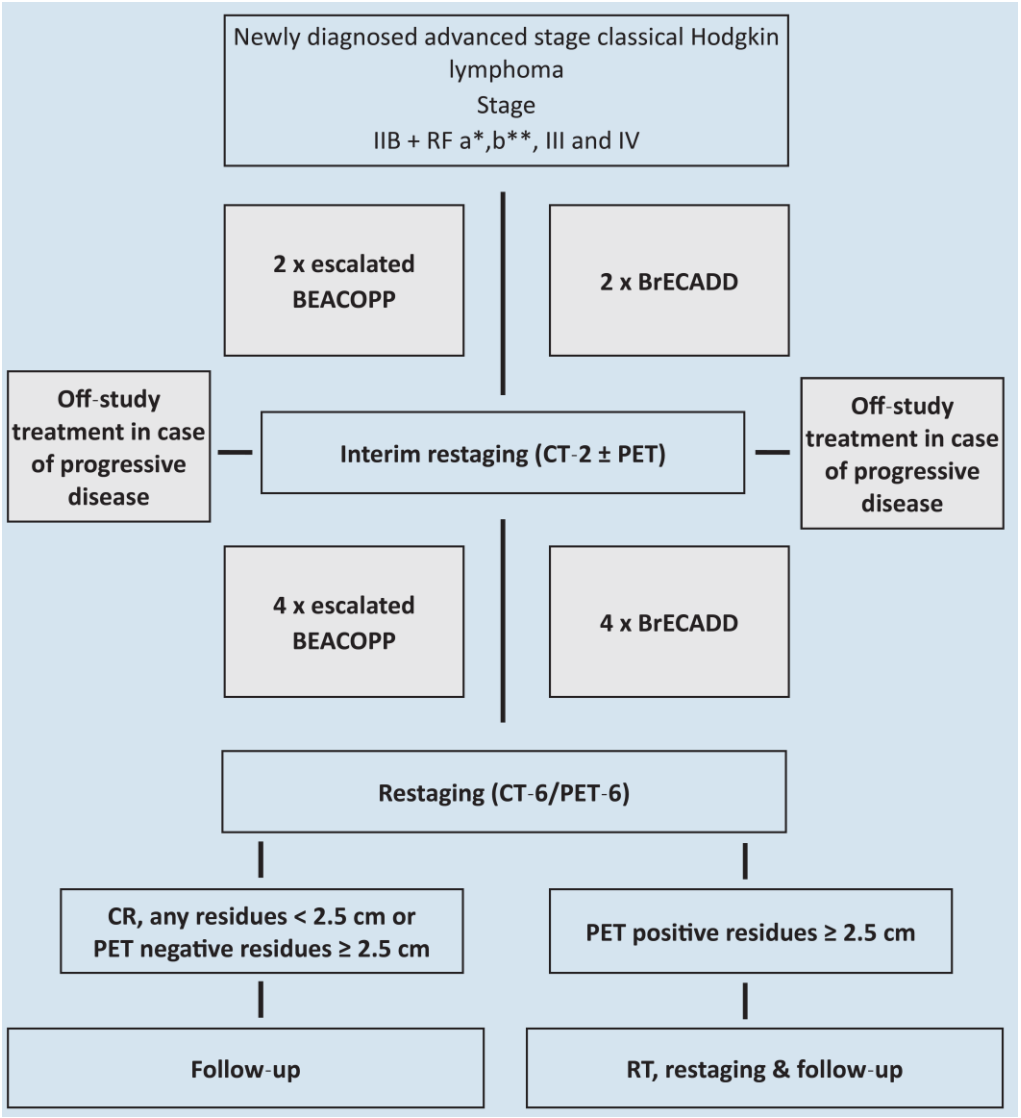
Eichenauer D, Lancet Oncol 2017

Schémas BrECADD/BrECAPP

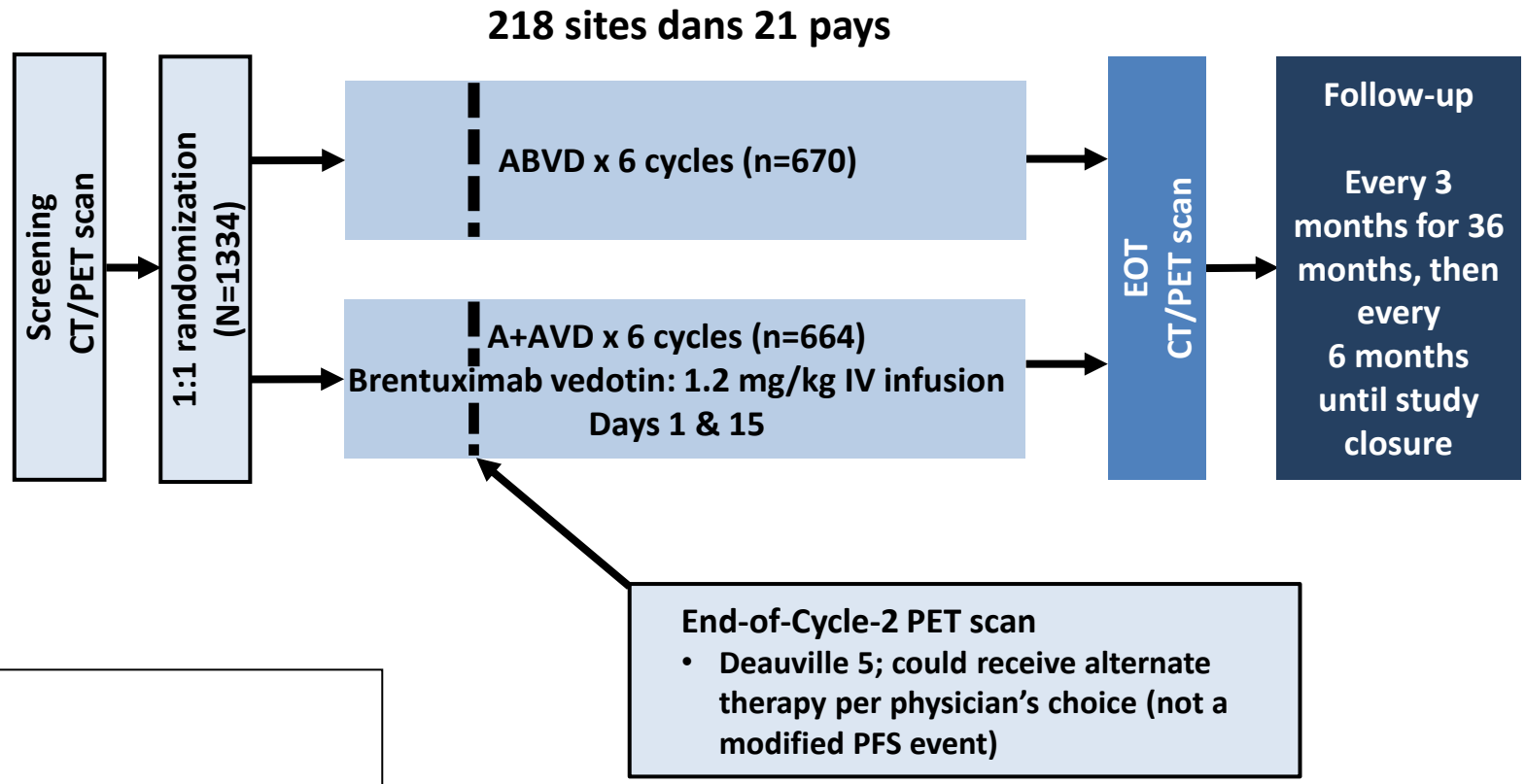
	BrECAPP (n=50)			BrECADD (n=52)		
	Grade 1–2	Grade 3	Grade 4	Grade 1–2	Grade 3	Grade 4
Any toxic effect	2 (4%)	7 (14%)	40 (80%)	3 (6%)	5 (10%)	41 (79%)
Haematological toxic effect	2 (4%)	6 (12%)	40 (80%)	4 (8%)	4 (8%)	41 (79%)
Anaemia	25 (50%)	19 (38%)	3 (6%)	29 (60%)	18 (35%)	0
Thrombocytopenia	12 (24%)	12 (24%)	20 (40%)	17 (32%)	12 (23%)	15 (29%)
Leukopenia	5 (10%)	4 (8%)	40 (80%)	8 (15%)	3 (6%)	41 (79%)
Drug fever	4 (8%)	1 (2%)	0	2 (4%)	0	0
Infection	7 (14%)	3 (6%)	1 (2%)	5 (10%)	7 (13%)	1 (2%)
Renal or urinary toxic effect*	0	0	0	3 (6%)	0	0
Hepatobiliary toxic effect*	4 (8%)	3 (6%)	1 (2%)	6 (12%)	1 (2%)	0
Nervous system, sensory	15 (30%)	1 (2%)	0	18 (35%)	0	0
Nervous system, motor	1 (2%)	0	0	0	0	0
Heart	0	0	0	0	0	0
Mucositis	10 (20%)	2 (4%)	0	7 (13%)	2 (4%)	0
Gastrointestinal tract	11 (22%)	2 (4%)	1 (2%)	16 (31%)	0	0
Urogenital tract	2 (4%)	0	0	2 (4%)	1 (2%)	0
Respiratory tract	5 (10%)	0	0	8 (15%)	0	0

Eichenauer D, Lancet Oncol 2017

Essai HD21 (en cours)



Essai Echelon 1

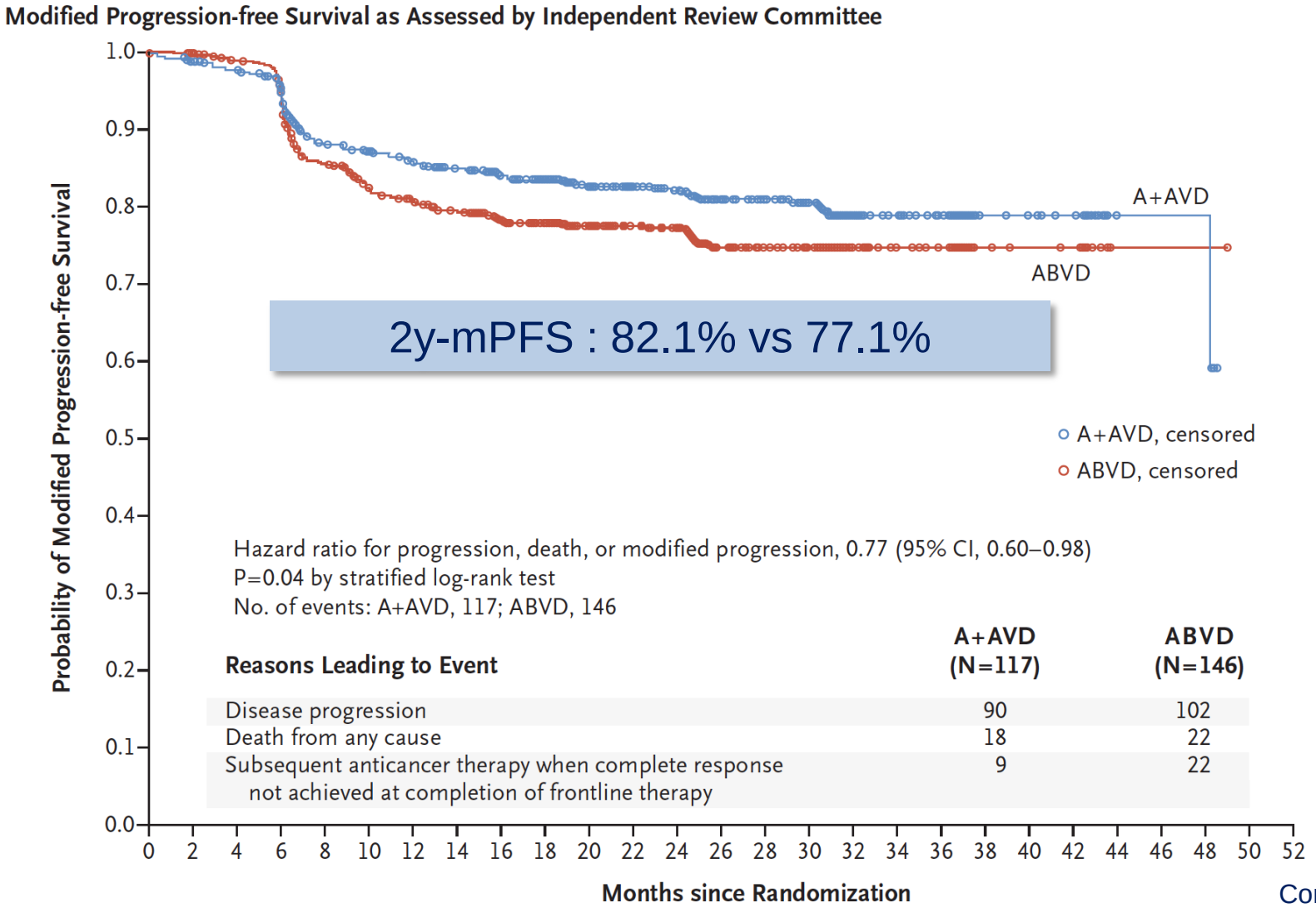


Inclusion criteria

- cHL stage III or IV
- ECOG PS 0, 1 or 2
- Age ≥18 years
- Measurable disease
- Adequate liver and renal function

Objectif principal : **PFS modifiée** (comprenant les TEP DS 3-5 avec un traitement complémentaire)

Essai Echelon 1



Connors J, ASH 2017 & NEJM 2018

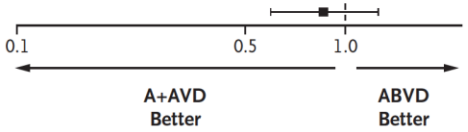
Essai Echelon 1

Patients with event, n (%)	A+AVD N=664	ABVD N=670	p-value†
CR rate* at end of randomized regimen	488 (73)	472 (70)	0.22
ORR* at end of randomized regimen	569 (86)	553 (83)	0.12
PET Deauville score 1 or 2 after completion of frontline therapy	563 (85)	537 (80)	0.03
PET Deauville score 1, 2, or 3 after cycle 2	588 (89)	577 (86)	0.18
PET Deauville score 4, or 5 after cycle 2			
4	26 (4)	28 (4)	
5	21 (3)	30 (4)	
Unavailable	29 (4)	35 (5)	

Connors J, ASH 2017 & NEJM 2018

Essai Echelon 1

Subgroup	A+AVD	ABVD	Hazard Ratio (95% CI)
	no. of events/total no. (%)		
Overall	117/664 (17.6)	146/670 (21.8)	0.77 (0.60–0.98)
Age			
<60 yr	93/580 (16.0)	117/568 (20.6)	0.73 (0.56–0.96)
≥60 yr	24/84 (28.6)	29/102 (28.4)	1.00 (0.58–1.72)
<65 yr	99/604 (16.4)	128/608 (21.1)	0.74 (0.57–0.96)
≥65 yr	18/60 (30.0)	18/62 (29.0)	1.01 (0.53–1.94)
<45 yr	70/451 (15.5)	83/423 (19.6)	0.73 (0.53–1.01)
≥45 yr	47/213 (22.1)	63/247 (25.5)	0.86 (0.59–1.25)
Geographic region			
Americas	41/261 (15.7)	58/262 (22.1)	0.65 (0.44–0.97)
North America	38/250 (15.2)	57/247 (23.1)	0.60 (0.40–0.90)
Europe	62/333 (18.6)	74/336 (22.0)	0.83 (0.59–1.17)
Asia	14/70 (20.0)	14/72 (19.4)	0.91 (0.43–1.94)
IPS			
0–1	22/141 (15.6)	25/141 (17.7)	0.84 (0.47–1.49)
2–3	57/354 (16.1)	68/351 (19.4)	0.79 (0.55–1.12)
4–7	38/169 (22.5)	53/178 (29.8)	0.70 (0.46–1.07)
Baseline Ann Arbor stage			
Stage III	40/237 (16.9)	43/246 (17.5)	0.92 (0.60–1.42)
Stage IV	77/425 (18.1)	102/421 (24.2)	0.71 (0.53–0.96)
Baseline B symptoms			
Yes	77/400 (19.3)	94/381 (24.7)	0.74 (0.55–1.01)
No	40/264 (15.2)	52/289 (18.0)	0.79 (0.52–1.20)
Baseline extranodal sites			
0	40/217 (18.4)	39/228 (17.1)	1.04 (0.67–1.62)
1	36/217 (16.6)	45/223 (20.2)	0.75 (0.48–1.16)
>1	39/194 (20.1)	57/193 (29.5)	0.67 (0.44–1.00)
Baseline ECOG status			
0	61/376 (16.2)	79/378 (20.9)	0.74 (0.53–1.03)
1	48/260 (18.5)	57/263 (21.7)	0.83 (0.56–1.21)
2	8/28 (28.6)	10/27 (37.0)	0.54 (0.21–1.38)
Sex			
Male	64/378 (16.9)	90/398 (22.6)	0.70 (0.51–0.97)
Female	53/286 (18.5)	56/272 (20.6)	0.86 (0.59–1.26)



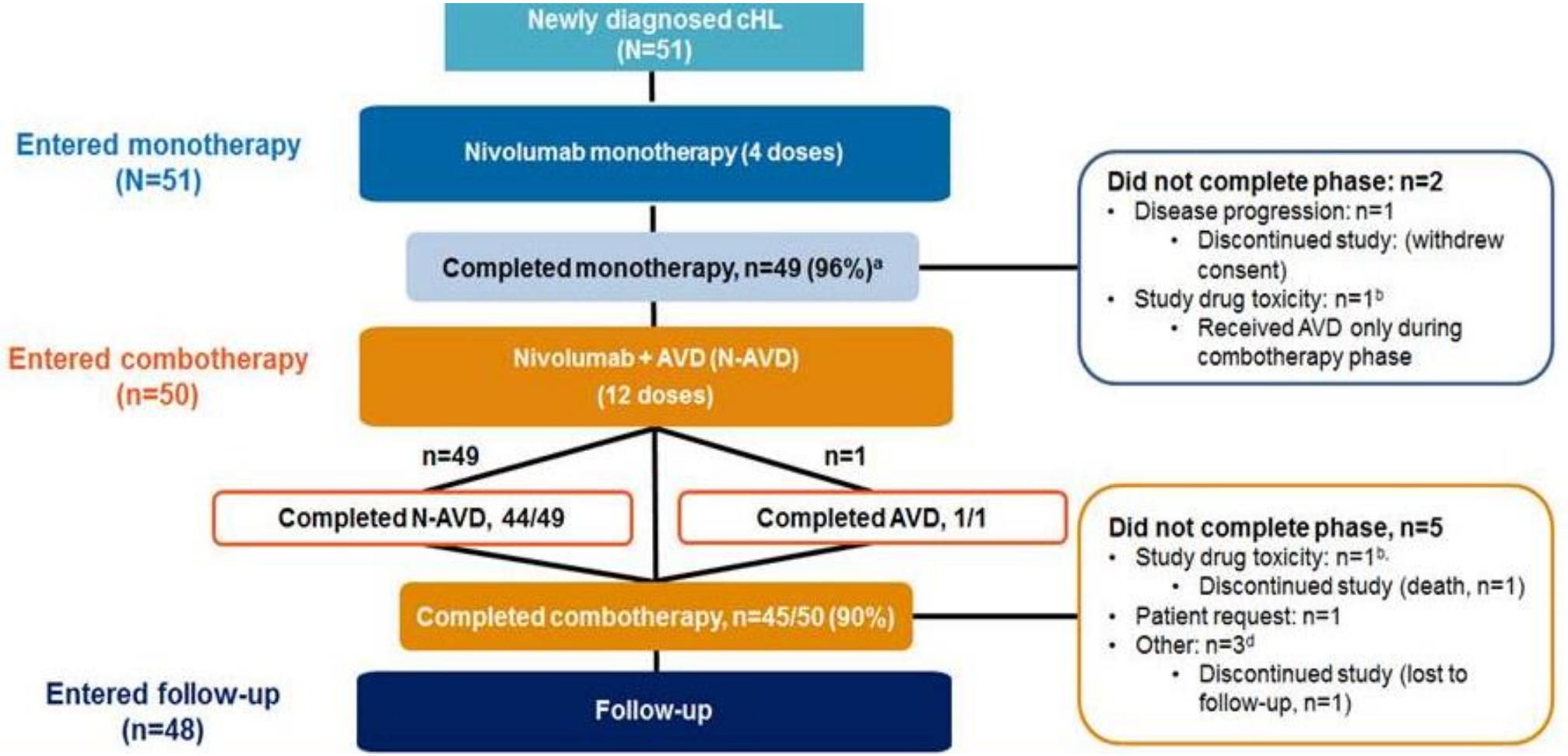
Connors J, ASH 2017 & NEJM 2018

Essai Echelon 1

Common adverse events, %*	A+AVD (N=662)		ABVD (N=659)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Neutropenia	58	54	45	39
Constipation	42	2	37	<1
Vomiting	33	3	28	1
Fatigue	32	3	32	1
Peripheral sensory neuropathy	29	5	17	<1
Diarrhea	27	3	18	<1
Pyrexia	27	3	22	2
Peripheral neuropathy	26	4	13	<1
Abdominal pain	21	3	10	<1
Stomatitis	21	2	16	<1
Febrile neutropenia	19	19	8	8

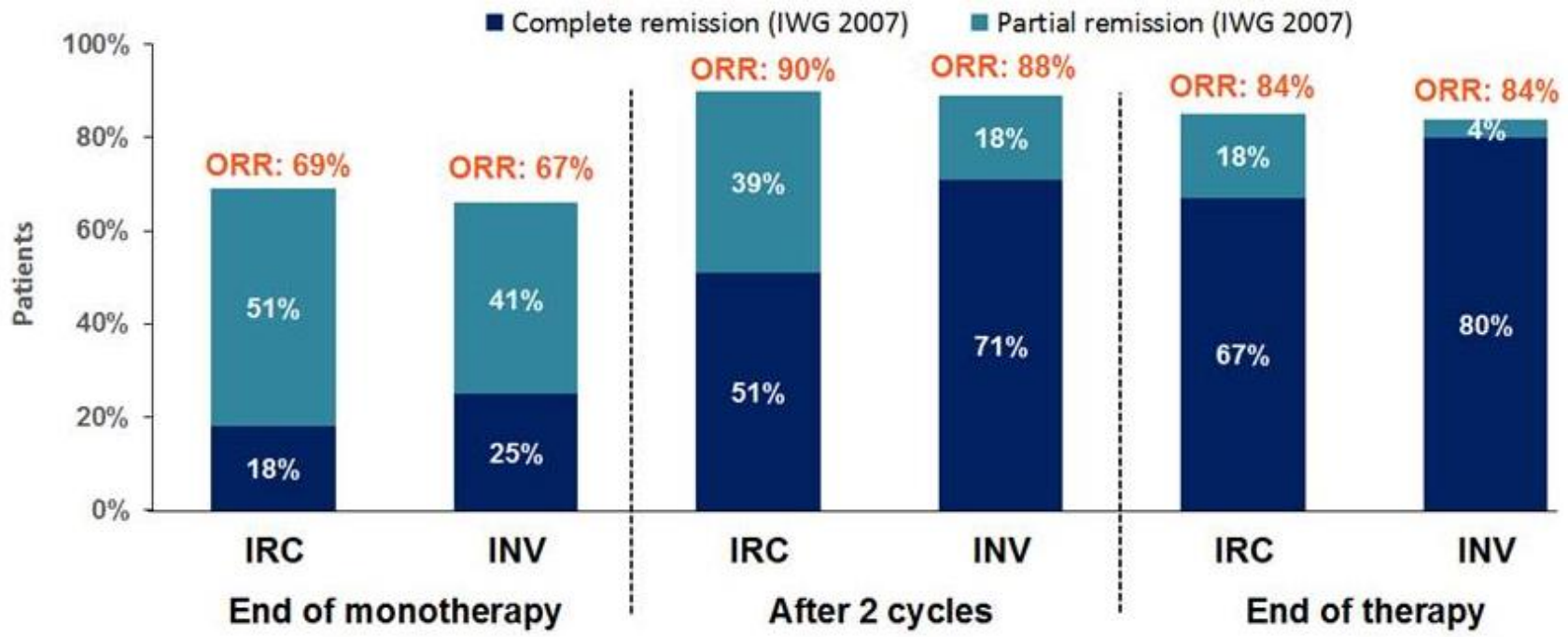
Connors J, ASH 2017 & NEJM 2018

Checkmate 205 – Cohorte D



Ramchandren R, ASH 2017

Checkmate 205 – Cohorte D



- At end of therapy, ORR per investigator for the ITT population was 84%, with 80% of patients achieving CR
- Five patients were non-evaluable at end of therapy

Ramchandren R, ASH 2017

Conclusions

- Les stratégies TEP-guidées permettent de réduire l'exposition au BEACOPP pour les patients TEP 2 négative après 2 cycles de BEACOPP
- **Importance des critères utilisés pour l'interprétation de la TEP**
- Le pronostic des patients avec une TEP 2 positive reste insatisfaisant : nouvelles stratégies d'intensifications thérapeutiques précoces ?
- La place des nouvelles drogues en 1ère ligne reste à préciser