白蛋白结合紫杉醇临床应用

山东大学齐鲁医院（青岛）

化疗科：孙颖

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NCCN Guidelines Version 8.202
Invasive Breast Cancer

PREOPERATIVE/ADJUVANT THERAPY

HER2-Positive[l,m,n]

Preferred Regimens:

- **Paclitaxel + trastuzumab[l,p]**
- **TCH (docetaxel/carboplatin/trastuzumab[l])**
- **TCHP (docetaxel/carboplatin/trastuzumab/pertuzumab[l])**
- **If no residual disease after preoperative therapy or no preoperative therapy: Comp trastuzumab[l] (category 1) ± pertuzumab.[q]**
- **If residual disease after preoperative therapy: Ado-trastuzumab emtansine (catego for toxicity, then trastuzumab[l] (category 1) ± pertuzumab to complete one year of t**

Useful in Certain Circumstances:

- **Docetaxel + cyclophosphamide + trastuzumab[l]**
- **AC followed by T[h] + trastuzumab[l,o] (doxorubicin/cyclophosphamide followed by paclitaxel plus trastuzumab, various schedules)**
- **AC followed by T[h] + trastuzumab[l] + pertuzumab[o] (doxorubicin/cyclophosphamide followed by paclitaxel plus trastuzumab plus pertuzumab, various schedules)**

Other Re

- **AC follo cyclop**
- **AC follo (doxoru trastuzu**

[a] Randomized clinical trials demonstrate that the addition of a taxane to anthracycline-based chemotherapy provides an improved outcome.
[b] CMF and RT may be given concurrently, or the CMF may be given first. All other chemotherapy regimens should be given prior to radiotherapy.
[c] Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy.
[d] Alternative taxanes (ie, docetaxel, paclitaxel, albumin-bound paclitaxel) may be substituted for select patients due to medical necessity (ie, hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of albumin-bound paclitaxel should not exceed 125 mg/m².
[e] Consider scalp cooling to reduce incidence of chemotherapy-induced alopecia for patients receiving chemotherapy. Results may be less effective with anthracycline-containing regimens.
[h] It is acceptable to change the administration sequence to taxane (with or without HER2 targeted therapy) followed by AC.
[l] An FDA-approved biosimilar is an appropriate substitute for trastuzumab.
[m] Trastuzumab and hyaluronidase-oysk injection for subcutaneous use may be substituted for trastuzumab. It has different dosage and administration instructions compared to intravenous trastuzumab. Do not substitute trastuzumab and hyaluronidase-oysk for or with ado-trastuzumab emtansine.
[n] Pertuzumab, t may be substi and intravenou trastuzumab, a dosing and ad
[o] Trastuzumab significant car anthracycline
[p] Paclitaxel + tr HER2-positive regimens due
[q] Consider exte therapy for pa risk of recurre patients who h
[r] Ado-trastuzum Minckwitz G, H HER2-positive

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participati

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PREOPERATIVE/ADJUVANT THERAPY REGIMENS[a,b,c,d,e]

HER2-Negative[f]

Preferred Regimens:

- **Dose-dense AC (doxorubicin/cyclophosphamide) followed by paclitaxel every 2 weeks[h]**
- **Dose-dense AC (doxorubicin/cyclophosphamide) followed by weekly paclitaxel[h]**
- **TC (docetaxel and cyclophosphamide)**
- **Olaparib, if germline *BRCA1/2* mutations[g,i]**
- **High-risk[j] triple-negative breast cancer (TNBC): Preoperative pembrolizumab + carboplatin + paclitaxel, followed by preoperative pembrolizumab + cyclophosphamide + doxorubicin or epirubicin, followed by adjuvant pembrolizumab**
- **TNBC and residual disease after preoperative therapy with taxane-, alkylator-, and anthracycline-based chemotherapy:[i] Capecitabine**

Useful in Certain Circumstances:

- **Dose-dense AC (doxorubicin/cyclophosphamide)**
- **AC (doxorubicin/cyclophosphamide) every 3 weeks (category 2B)**
- **CMF (cyclophosphamide/methotrexate/fluorouracil)**
- **AC followed by weekly paclitaxel[h]**

Other Recommended Regimens:

- **AC followed by docetaxel every 3 weeks[h]**
- **EC (epirubicin/cyclophosphamide)**
- **TAC (docetaxel/doxorubicin/cyclophosphamide)**
- **Select patients with TNBC in the preoperative setting only:[k]**
  - **Weekly paclitaxel + carboplatin[k]**
  - **Docetaxel + carboplatin[k]**

[a] Randomized clinical trials demonstrate that the addition of a taxane to anthracycline-based chemotherapy provides an improved outcome.
[b] CMF and RT may be given concurrently, or the CMF may be given first. All other chemotherapy regimens should be given prior to radiotherapy.
[c] Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy.
[d] Alternative taxanes (ie, docetaxel, paclitaxel, albumin-bound paclitaxel) may be substituted for select patients due to medical necessity (ie, hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of albumin-bound paclitaxel should not exceed 125 mg/m².
[e] Consider scalp cooling to reduce incidence of chemotherapy-induced alopecia for patients receiving neoadjuvant/adjuvant chemotherapy. Results may be less effective with anthracycline-containing regimens.
[f] The regimens listed in the table for HER2-negative disease are all category 1 (except where indicated) when used in the adjuvant setting.
[g] Consider addition of adjuvant olaparib for 1 y for those with germline *BRCA1/2* mutations and:
- TNBC, if 1) ≥pT2 or ≥pN1 disease after adjuvant chemotherapy, or 2) residual disease after preoperative chemotherapy
- HR-positive, HER2-negative tumors, if 1) ≥4 positive lymph nodes after adjuvant chemotherapy (category 2A), or 2) residual disease after preoperative therapy and a clinical stage, pathologic stage, estrogen receptor status, and tumor grade (CPS+EG) score ≥3 (category 2A).

Adjuvant olaparib can be used concurrently with endocrine therapy.

[h] It is acceptable to change the administration sequence to taxane (with or without HER2 targeted therapy) followed by AC.
[i] The patients in OlympiA trial did not receive capecitabine, thus there is no data on sequencing or to guide selection of one over the other.
[j] High-risk criteria include stage II-III TNBC. The use of adjuvant pembrolizumab (category 2A) may be individualized.
[k] The inclusion of platinum agents as neoadjuvant chemotherapy for TNBC remains controversial. Several studies have shown improved pCR rates with incorporation of platinum. However, long-term outcomes remain unknown. The routine use of platinum agents as part of neoadjuvant therapy for TNBC is not recommended for most patients (including *BRCA* mutation carriers), but it may be considered in select patients (such as those for whom achieving better local control is necessary). The use of platinum agents in the adjuvant setting is not recommended. If platinum agents are included in an anthracycline-based regimen, the optimal sequence of chemotherapy and choice of taxane agent is not established.

（三）HER-2 阳性乳腺癌新辅助治疗[1]

Ⅰ级推荐	Ⅱ级推荐
1. TCbHP[4]（1A） 2. THP[3]（1A）	1. 抗 HER-2 单抗联合紫杉类为基础的其他方案（2B） 如 TCbH[2]（2A）、AC-THP[5]（2B） 2. 科学、合理设计的临床研究

注：T. 紫杉类，包括多西他赛、白蛋白紫杉醇[6]、紫杉醇
A. 蒽环类[7]，包括表柔比星、吡柔比星、多柔比星
C. 环磷酰胺
Cb. 卡铂
H. 曲妥珠单抗
P. 帕妥珠单抗

1. 激素受体阳性乳腺癌新辅助化疗

Ⅰ级推荐	Ⅱ级推荐
蒽环联合紫杉方案 TAC 方案（1A） AT 方案（2A）	以蒽环和紫杉为主的其他方案 AC-T 方案（1B）

注：T：紫杉类，包括多西他赛、白蛋白紫杉醇[4]、紫杉醇
A：蒽环类，包括表柔比星、吡柔比星、多柔比星
C：环磷酰胺

新辅助化疗注释及剂量推荐详见“（四）三阴性乳腺癌新辅助治疗”。

（四）三阴性乳腺癌新辅助治疗

Ⅰ级推荐	Ⅱ级推荐
1. 蒽环联合紫杉方案[1] TAC（1A） AT（2A） 2. TP[2, 3]（2A）	1. AC-T（1B） 2. 参加严格设计的临床研究， 如含白蛋白紫杉醇联合 PD-1/PD-L1 抑制剂

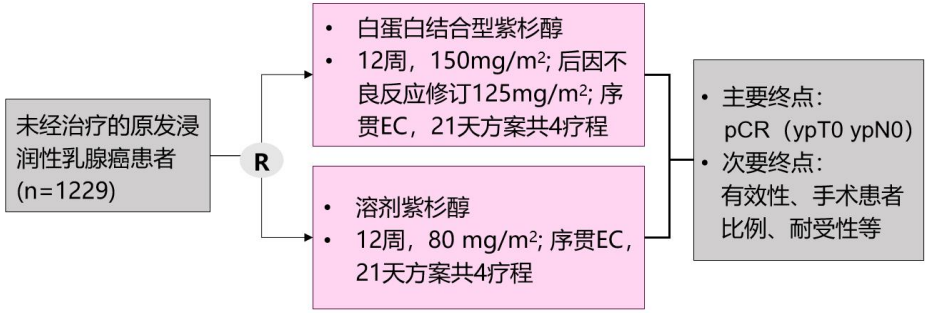
注：T. 紫杉类，包括多西他赛、白蛋白紫杉醇[4]、紫杉醇
A. 蒽环类，包括表柔比星、吡柔比星[5]、多柔比星
C. 环磷酰胺
P. 铂类

TP（紫杉联合铂类）			
白蛋白紫杉醇	125mg/m^2	d1、8	1/21d×6
顺铂	75mg/m^2	分 d1~3	
TP（紫杉联合铂类）			
白蛋白紫杉醇	125mg/m^2	d1、8	1/21d×6
卡铂	AUC 6	d1	

GBG69 研究[13]结果提示，新辅助治疗中白蛋白紫杉醇比溶剂型紫杉醇有更高的 pCR 率，同时能够改善患者 DFS，因此新辅助治疗中也可以选用。

新辅助 GBG69研究

- 纳米白蛋白紫杉醇对比溶剂型紫杉醇用于**早期乳腺癌**新辅助化疗的III期随机对照临床试验



注：EC方案包括：表柔比星 90 mg/m² +环磷酰胺 600mg/m²

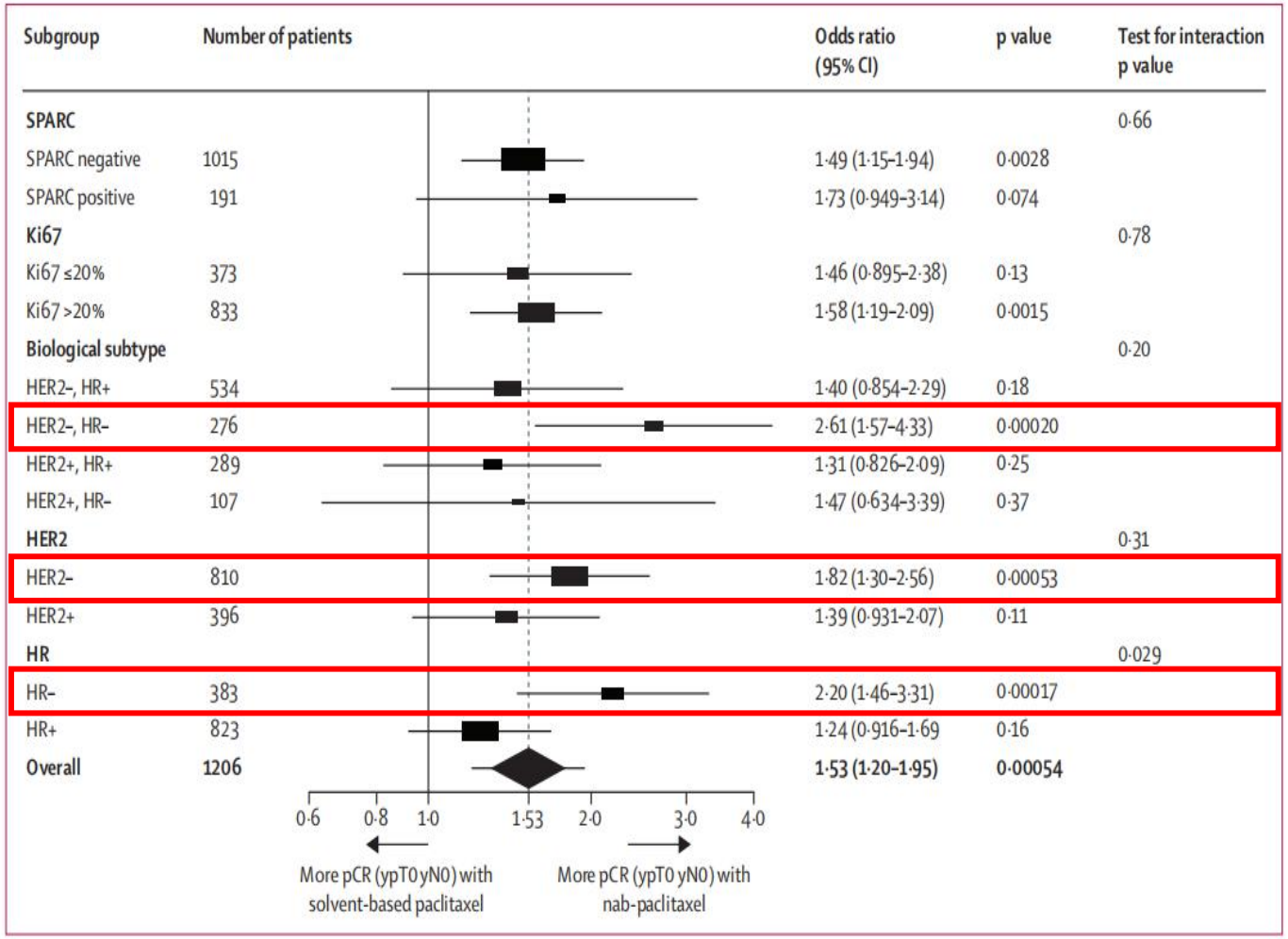
✓ 对于HER2阳性患者需联合曲妥珠单抗和帕妥珠单抗化疗。

✓ 分层因素包括：激素受体、HER2状态、Ki-67表达、SPARC表达。

	Nab-paclitaxel (n=606)	Solvent-based paclitaxel (n=600)	Nab-paclitaxel vs solvent-based paclitaxel	
			OR (95% CI)	Unadjusted p value*
ypT0 ypN0				
Yes	233 (38·4%; 34·6–42·3)	174 (29·0%; 25·4–32·6)	1·53 (1·20–1·95)	0·00065
Before March 28, 2013				
Yes	77 (33·6%; 27·5–39·7)	53 (23·5%; 17·9–29·0)	1·65 (1·10–2·50)	0·022
After March 28, 2013				
Yes	156 (41·4%; 36·4–46·4)	121 (32·4%; 27·6–37·1)	1·48 (1·10–1·99)	0·013

提高了接近10%PCR率。

Nab-paclitaxel versus solvent-based paclitaxel in neoadjuvant chemotherapy for early breast cancer (GeparSepto—GBG 69): a randomised, phase 3 trial



GBG69研究 不良反应评估

	Nab-paclitaxel (n=605)*				Solvent-based paclitaxel (n=601)*				p value grade 1–5	p value grade 3–5
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5		
Anaemia	547 (90%)	12 (2%)	1 (<1%)	0	524 (87%)	4 (1%)	0	0	0·011	0·048
Leucopenia	287 (47%)	224 (37%)	56 (9%)	0	279 (47%)	219 (37%)	52 (9%)	0	0·22	0·73
Neutropenia	163 (27%)	139 (23%)	229 (38%)	0	116 (19%)	153 (25%)	218 (36%)	0	0·0018	0·72
Febrile neutropenia	..	20 (3%)	8 (1%)	0	..	19 (3%)	5 (1%)	0	..	0·67
Lymphopenia	170 (46%)	46 (12%)	20 (5%)	0	165 (44%)	41 (11%)	14 (4%)	0	0·099	0·23
Thrombopenia	139 (23%)	3 (<1%)	2 (<1%)	0	142 (24%)	2 (<1%)	1 (<1%)	0	0·89	0·73
Increased alkaline phosphatase	141 (23%)	1 (<1%)	1 (<1%)	0	123 (20%)	0	0	0	0·21	0·50
Increased aspartate aminotransferase	228 (38%)	5 (1%)	1 (<1%)	0	211 (35%)	4 (1%)	0	0	0·34	0·75
Increased alanine aminotransferase	322 (53%)	14 (2%)	1 (<1%)	0	328 (55%)	12 (2%)	0	0	0·73	0·70
Fatigue	462 (76%)	30 (5%)	..	..	431 (72%)	25 (4%)	..	..	0·025	0·58
Headache	183 (30%)	4 (1%)	..	..	168 (28%)	5 (1%)	..	..	0·45	0·75
Nausea	410 (68%)	16 (3%)	..	..	411 (68%)	14 (2%)	..	..	0·95	0·85
Vomiting	138 (23%)	5 (1%)	2 (<1%)	0	130 (22%)	9 (1%)	1 (<1%)	0	0·79	0·48
Mucositis, stomatitis, or oesophagitis	299 (49%)	6 (1%)	1 (<1%)	0	284 (47%)	5 (1%)	0	0	0·39	0·77
Diarrhoea	289 (48%)	19 (3%)	0	1 (<1%)	248 (41%)	14 (2%)	3 (<1%)	0	0·016	0·74
Anorexia	107 (18%)	4 (1%)	0	0	103 (17%)	1 (<1%)	0	0	0·65	0·37
Hypotension	66 (11%)	0	0	0	50 (8%)	0	0	0	0·14	..
Alopecia	565 (93%)	..	..	..	561 (93%)	..	..	..	1·00	..
Skin rash maculopapular	195 (32%)	7 (1%)	..	..	139 (23%)	4 (1%)	..	..	0·00028	0·55
Hand–foot syndrome	158 (26%)	13 (2%)	..	..	101 (17%)	6 (1%)	..	..	<0·0001	0·16
Allergic reactions	98 (16%)	3 (<1%)	0	0	120 (20%)	5 (1%)	0	0	0·076	0·51
Peripheral sensory neuropathy	451 (75%)	59 (10%)	4 (1%)	0	376 (63%)	16 (3%)	0	0	<0·0001	<0·0001
Arthralgia	218 (36%)	5 (1%)	..	..	206 (34%)	1 (<1%)	..	..	0·40	0·22
Myalgia	185 (31%)	2 (<1%)	..	..	150 (25%)	0	..	..	0·025	0·50
Epistaxis	225 (37%)	0	0	0	221 (37%)	0	0	0	0·91	..
Dyspnoea	97 (16%)	5 (1%)	0	0	97 (16%)	7 (1%)	2 (<1%)	0	0·76	0·30
Fever without neutropenia	103 (17%)	5 (1%)	2 (<1%)	0	94 (16%)	7 (1%)	1 (<1%)	0	0·60	0·80
Infection	272 (45%)	32 (5%)	4 (1%)	1 (<1%)	252 (42%)	34 (6%)	2 (<1%)	0	0·27	1·00
Anaphylaxis†	..	1 (<1%)	0	0	..	1 (<1%)	1 (<1%)	0	..	0·62
Congestive heart failure, according to NYHA‡	2 (<1%)	1 (<1%)	0	0	1 (<1%)	0	1 (<1%)	1 (<1%)	1·00	0·62
Other non-haematological adverse events	442 (73%)	98 (16%)	14 (2%)	1 (<1%)	449 (75%)	66 (11%)	13 (2%)	0	0·024	0·0094

Data are n (valid %) unless otherwise stated. Valid % was calculated based on available data only. All given adverse events were predefined. *"Other non-haematological adverse events" were those reported as free text. Data not provided for grades that do not exist under the Common Terminology Criteria for Adverse Events for the respective condition (eg, grade >3 for fatigue). NYHA=New York Heart Association. *One patient randomised to nab-paclitaxel received solvent-based paditaxel, so is included in this group for the safety analysis. †Adverse event of special interest. ‡Adverse event of special interest, if NYHA 3–4.

Table 3: Adverse events

3,4级神经毒性发生率

Findings Between July 30, 2012, and Dec 23, 2013, we randomly assigned 1229 women, of whom 1206 started treatment (606 with nab-paclitaxel and 600 with solvent-based paclitaxel). The nab-paclitaxel dose was reduced after enrolment of 464 participants to 125 mg/m² due to increased treatment discontinuation and sensory neuropathy in this group. Pathological complete response occurred more frequently in the nab-paclitaxel group (233 [38%, 95% CI 35–42] patients) than in the solvent-based paclitaxel group (174 [29%, 25–33] patients; OR 1·53, 95% CI 1·20–1·95; unadjusted p=0·00065). The incidence of grade 3–4 anaemia (13 [2%] of 605 patients in the nab-paclitaxel group vs four [1%] of patients in the solvent-based paclitaxel group; p=0·048) and peripheral sensory neuropathy grade 3–4 (63 [10%] patients receiving any nab-paclitaxel dose; 31 [8%] of patients starting with 125 mg/m² and 32 [15%] of patients starting with 150 mg/m²; vs 16 [3%] in the solvent-based paclitaxel group, p<0·001) was significantly higher for nab-paclitaxel than for solvent-based paclitaxel. Overall, 283 (23%) patients were noted to have at least one serious adverse event (based on study drug received), 156 (26%) in the nab-paclitaxel group and 127 (21%) in the solvent-based paclitaxel group (p=0·057). There were three deaths (during epirubicin plus cyclophosphamide treatment) in the nab-paclitaxel group (due to sepsis, diarrhoea, and accident unrelated to the trial) versus one in the solvent-based paclitaxel group (during paclitaxel treatment; cardiac failure).

白紫	125mg/M2 8% 150mg/M2 15%	10%
紫杉醇		3%

original report

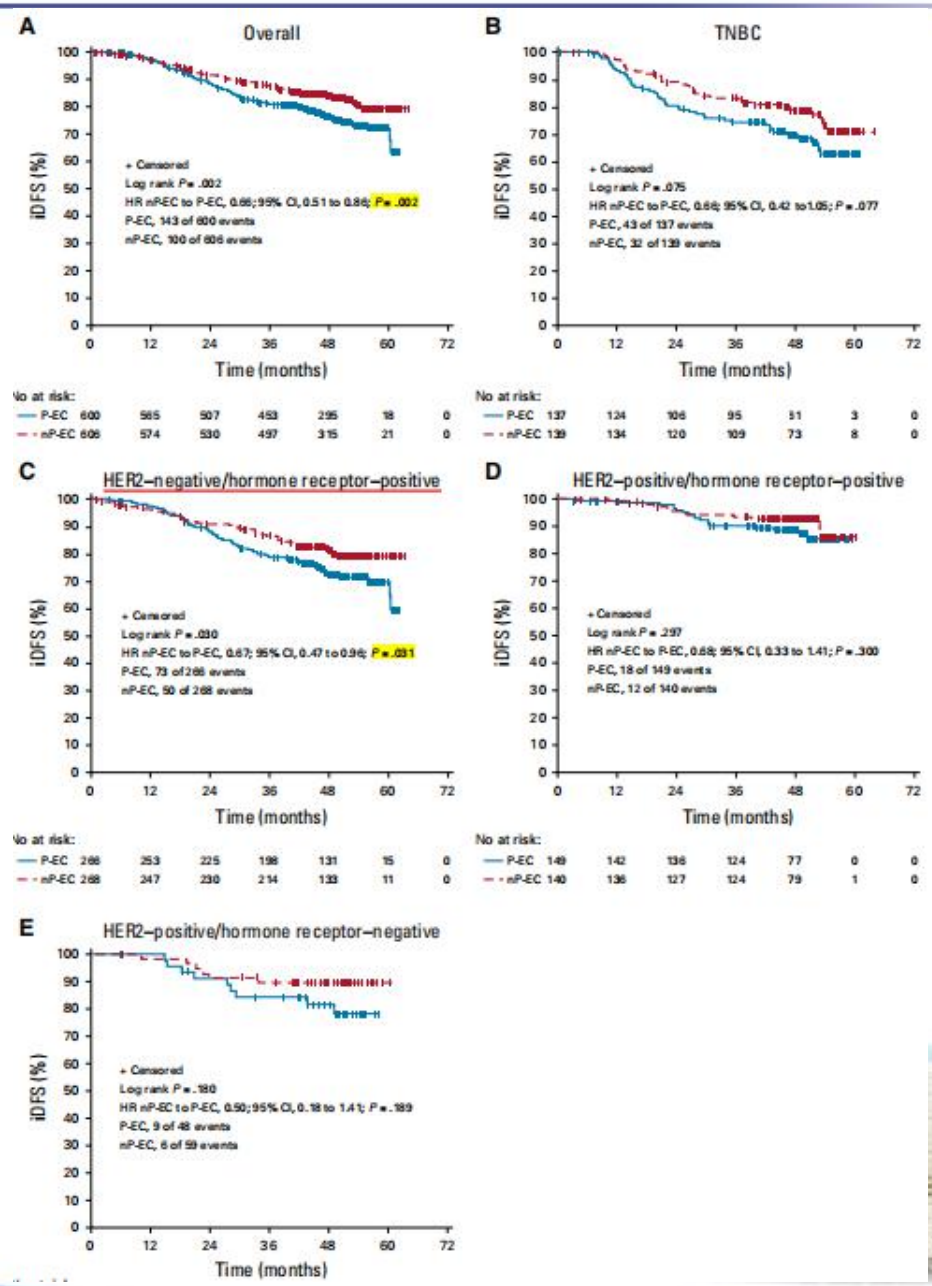
NAB-Paclitaxel Improves Disease-Free Survival in Early Breast Cancer: GBG 69–GeparSepto

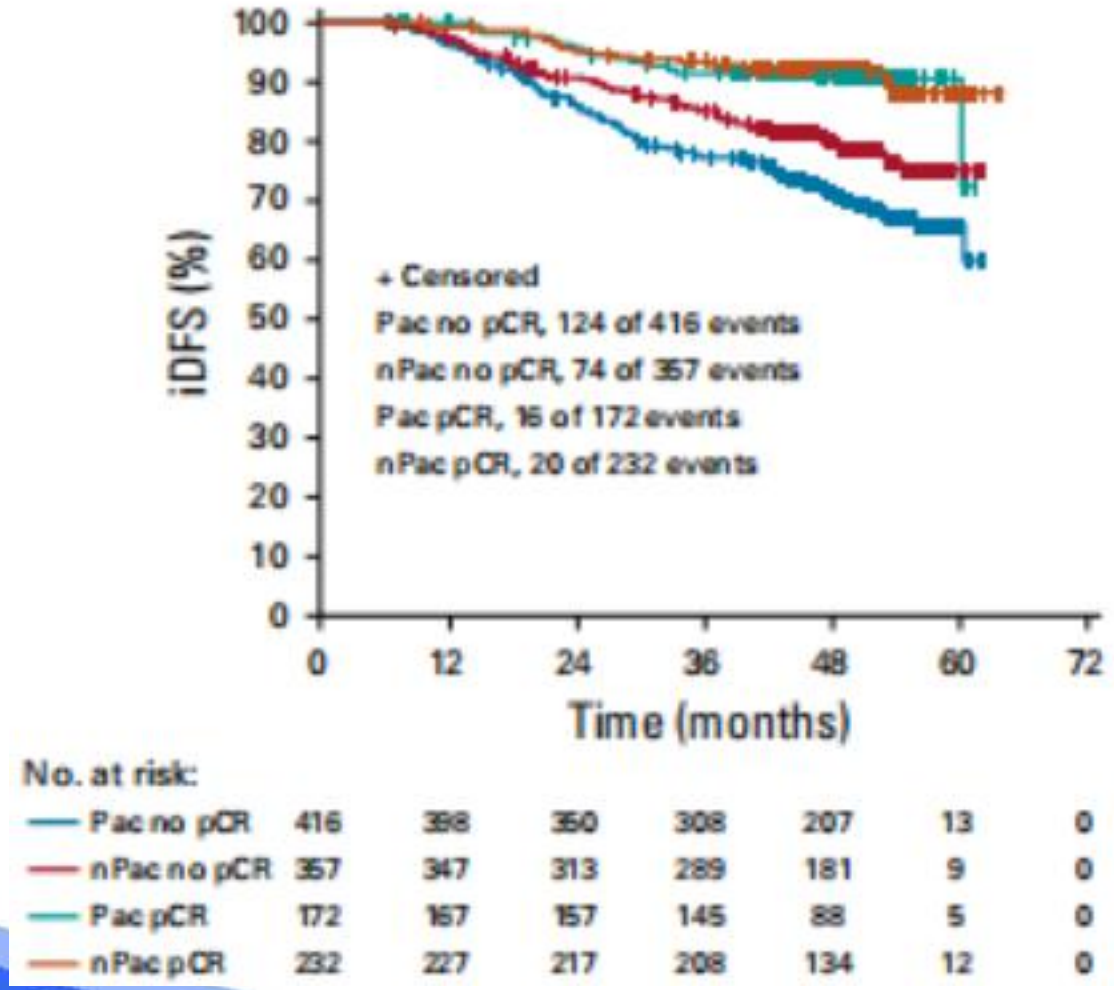
Michael Untch, MD, PhD[1]; Christian Jackisch, MD, PhD[2]; Andreas Schneeweiss, MD[3]; Sabine Schmatloch, MD[4]; Bahriye Aktas, MD[5]; Carsten Denkert, MD[6]; Christian Schem, MD, PhD, MaHM[7]; Hermann Wiebringhaus, MD[8]; Sherko Kümmel, PhD[9]; Mathias Warm, PhD[10]; Peter A. Fasching, MD[11]; Marianne Just, MD[12]; Claus Hanusch, MD[13]; John Hackmann, MD[14]; Jens-Uwe Blohmer, MD, PhD[15]; Kerstin Rhiem, MD[16]; Wolfgang D. Schmitt, MD[6]; Jenny Furlanetto, MD[17]; Bernd Gerber, PhD[18]; Jens Huober, MD[19]; Valentina Nekljudova, PhD[17]; Gunter von Minckwitz, MD[17]; and Sibylle Loibl, MD, PhD[17]

RESULTS A total of 1,206 patients started treatment, 606 with NAB-paclitaxel and 600 with sb-paclitaxel. After a median follow-up of 49.6 months (range, 0.5 to 64.0 months), 243 invasive disease–free survival (iDFS) events were reported (143 in the sb-paclitaxel and 100 in the NAB-paclitaxel arm). At 4 years, overall patients treated with NAB-paclitaxel had a significantly better iDFS compared with sb-paclitaxel (84.0% *v* 76.3%; hazard ratio, 0.66; 95% CI, 0.51 to 0.86; $P = .002$), whereas overall survival did not significantly differ between the two treatment arms (89.7% *v* 87.2%, respectively; hazard ratio, 0.82; 95% CI, 0.59 to 1.16; $P = .260$). Long-term follow-up of the treatment-related peripheral sensory neuropathy (PSN) showed a significant decrease of the median time to resolve PSN after NAB-paclitaxel 125 mg/m² compared with NAB-paclitaxel 150 mg/m².

ITT
HR+ HER-2 (-)

	4年 DFS	
白紫	84.0%	P=0.002
紫杉醇	76.3%	





神经毒性恢复至1级时间

Overall, 355 of 1,206 (29.4%) patients reported grade 2-4 PSN and 80 of 1,206 (6.6%) grade 3-4 during study treatment[12] (Appendix Table A4, online only). After a median follow-up of 220.1 weeks (range, 7.7 to 290 weeks), the median time to resolve grade 2-4 PSN to grade 1 was statistically significantly longer in patients after NAB-paclitaxel 150 mg/m^2 versus after NAB-paclitaxel 125 mg/m^2 treatment (12.7 weeks; 95% CI, 8.9 to 16.0 weeks; *v* 6.4 weeks; 95% CI, 4.1 to 10.0 weeks; log-rank $P = .014$, respectively), whereas no statistically significant difference was observed for patients treated with sb-paclitaxel (7.0 weeks; 95% CI, 6.0 to 9.0 weeks) versus NAB-paclitaxel 125 mg/m^2 (log-rank $P = .740$). The median time to resolve grade 3-4 PSN to grade 1 did not statistically significantly differ either between NAB-paclitaxel 150 mg/m^2 (157.3 weeks; 95% CI, 11.6 to 209.1 weeks) and 125 mg/m^2 (32.0 weeks; 95% CI, 6.0 to 135.7 weeks; log-rank $P = .200$) or between sb-paclitaxel (10.4 weeks; 95% CI, 5.0 to 123.3 weeks) and NAB-paclitaxel 125 mg/m^2 (log-rank $P = .161$; Appendix Fig A5, online only).

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SYSTEMIC THERAPY REGIMENS FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE[a,b,c]

HER2-Negative

Preferred Regimens

- Anthracyclines
  - Doxorubicin
  - Liposomal doxorubicin
- Taxanes
  - Paclitaxel
- Anti-metabolites
  - Capecitabine
  - Gemcitabine
- Microtubule inhibitors
  - Vinorelbine
  - Eribulin
- Sacituzumab govitecan-hziy (for TNBC)[g]
- For germline *BRCA1/2* mutations[d] see additional targeted therapy options (BINV-R)[e]
- Platinum (for TNBC and germline *BRCA1/2* mutation)[d]
  - Carboplatin
  - Cisplatin
- For PD-L1–positive TNBC see additional targeted therapy options (BINV-R)[e]

Other Recommended Regimens[f]

- Cyclophosphamide
- Docetaxel
- Albumin-bound paclitaxel
- Epirubicin
- Ixabepilone

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Invasive Breast Cancer

SYSTEMIC THERAPY REGIMENS FOR RECURRENT UNRESECTABLE (LOC

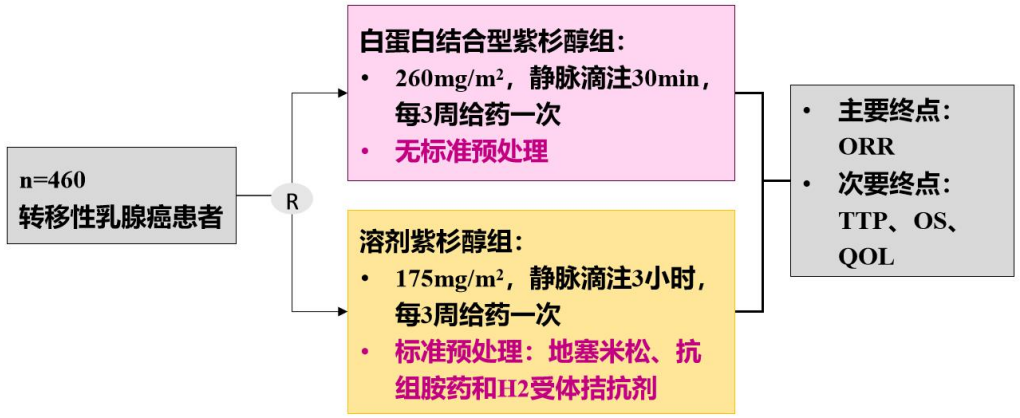
HER2-Negative Regimens:

- **Anthracyclines:**
  - Doxorubicin 60–75 mg/m² IV day 1; cycled every 21 days[1]
  - Doxorubicin 20 mg/m² IV day 1 weekly[2]
  - Liposomal doxorubicin[3] 50 mg/m² IV day 1; cycled every 28 days
- **Taxanes:**
  - Paclitaxel 175 mg/m² IV day 1; cycled every 21 days[4]
  - Paclitaxel 80 mg/m² IV day 1 weekly[5]
- **Antimetabolites:**
  - Capecitabine[6] 1000–1250 mg/m² PO twice daily days 1–14; cycled every 21 days
  - Gemcitabine[7] 800–1200 mg/m² IV days 1, 8, and 15; cycled every 28 days
- **Microtubule inhibitors:**
  - Vinorelbine[8,9]
    - 25 mg/m² IV day 1 weekly; or
    - 20–35 mg/m² IV days 1 and 8; cycled every 21 days; or
    - 25–30 mg/m² IV days 1, 8, and 15; cycled every 28 days
  - Eribulin[10] 1.4 mg/m² IV days 1 and 8; cycled every 21 days
- **Platinum (for TNBC and germline *BRCA1/2* mutation)**
  - Carboplatin[11] AUC 6 IV on day 1
    - Cycled every 21–28 days
  - Cisplatin[12] 75 mg/m² IV on day 1
    - Cycled every 21 days
- **Cyclophosphamide[13]**
  - 50 mg PO daily on days 1–21
  - Cycled every 28 days
- **Docetaxel[14,15]**
  - 60–100 mg/m² IV day 1
  - Cycled every 21 days
- **Docetaxel[16]**
  - 35 mg/m² IV weekly for 6 weeks followed by a 2-week rest, then repeat
- **Albumin-bound paclitaxel[17,18]**
  - 100 mg/m² or 125 mg/m² IV days 1, 8, and 15
  - Cycled every 28 days
- **Albumin-bound paclitaxel[17]**
  - 260 mg/m² IV
  - Cycled every 21 days
- **Epirubicin[19]**
  - 60–90 mg/m² IV day 1
  - Cycled every 21 days
- **Ixabepilone[20]**
  - 40 mg/m² IV day 1
  - Cycled every 21 days
- **Sacituzumab govitecan-hziy (for TNBC)[21]**
  - 10 mg/kg IV on days 1 and 8
  - Cycled every 21 days

VOLUME 23 · NUMBER 31 · NOVEMBER 1 2005
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

Phase III Trial of Nanoparticle Albumin-Bound Paclitaxel Compared With Polyethylated Castor Oil–Based Paclitaxel in Women With Breast Cancer

William J. Gradishar, Sergei Tjulandin, Neville Davidson, Heather Shaw, Neil Desai, Paul Bhar, Michael Hawkins, and Joyce O'Shaughnessy



Results

ABI-007 demonstrated significantly higher response rates compared with standard paclitaxel (33% *v* 19%, respectively; $P = .001$) and significantly longer time to tumor progression (23.0 *v* 16.9 weeks, respectively; hazard ratio = 0.75; $P = .006$). The incidence of grade 4 neutropenia was significantly lower for ABI-007 compared with standard paclitaxel (9% *v* 22%, respectively; $P < .001$) despite a 49% higher paclitaxel dose. Febrile neutropenia was uncommon (< 2%), and the incidence did not differ between the two study arms. Grade 3 sensory neuropathy was more common in the ABI-007 arm than in the standard paclitaxel arm (10% *v* 2%, respectively; $P < .001$) but was easily managed and improved rapidly (median, 22 days). No hypersensitivity reactions occurred with ABI-007 despite the absence of premedication and shorter administration time.

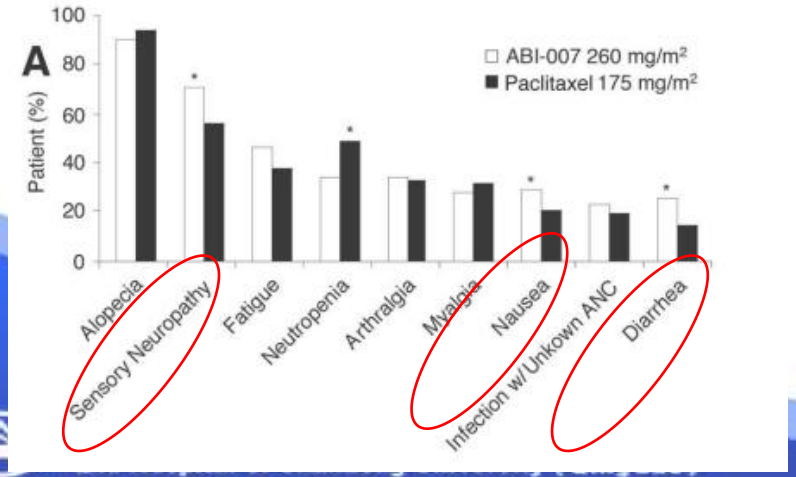
晚期研究　白紫与紫杉醇脂质体

Table 2. Response Rates

Response	ABI-007 (260 mg/m²) No. of Patients/Total No. of Patients	%	95% CI (%)	Standard Paclitaxel (175 mg/m²) No. of Patients/Total No. of Patients	%	95% CI (%)	P
Complete and partial response							
All patients	76/229	33	27.09 to 39.29	42/225	19	13.58 to 23.76	.001
First-line therapy	41/97	42	32.44 to 52.10	24/89	27	17.75 to 36.19	.029
Second-line or greater therapy	35/132	27	18.98 to 34.05	18/136	13	7.54 to 18.93	.006
Prior anthracycline therapy							
Adjuvant and/or metastatic	60/176	34	27.09 to 41.09	32/175	18	12.56 to 24.01	.002
Metastatic only	31/115	27	18.85 to 35.07	18/130	14	7.91 to 19.78	.010
Dominant metastatic organ site							
Visceral	59/176	34	26.55 to 40.50	34/182	19	13.02 to 24.34	.002
Nonvisceral	17/50	34	20.87 to 47.13	8/43	19	6.97 to 30.24	NS
Age, years							
< 65	68/199	34	27.58 to 40.76	36/193	19	13.16 to 24.15	< .001
≥ 65	8/30	27	10.84 to 42.49	6/32	19	5.23 to 32.27	NS

Abbreviation: NS, not significant statistically.

ORR提高了14%



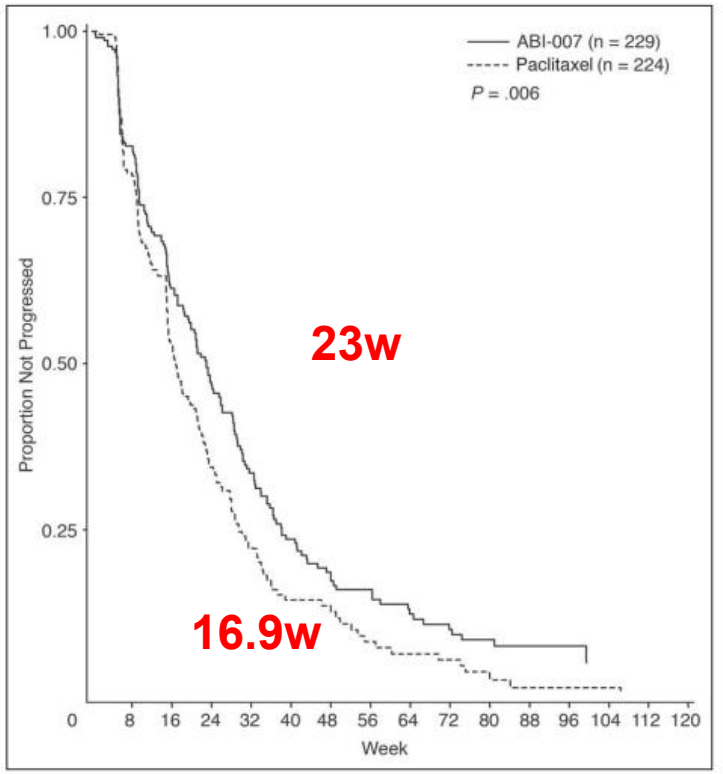


Fig 1. Median time to disease progression.

VOLUME 27 · NUMBER 22 · AUGUST 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Significantly Longer Progression-Free Survival With *nab*-Paclitaxel Compared With Docetaxel As First-Line Therapy for Metastatic Breast Cancer

William J. Gradishar, Dimitry Krasnojon, Sergey Cheporov, Anatoly N. Makhson, Georgiy M. Manikhas, Alicia Clawson, and Paul Bhar

A B S T R A C T

Patients and Methods

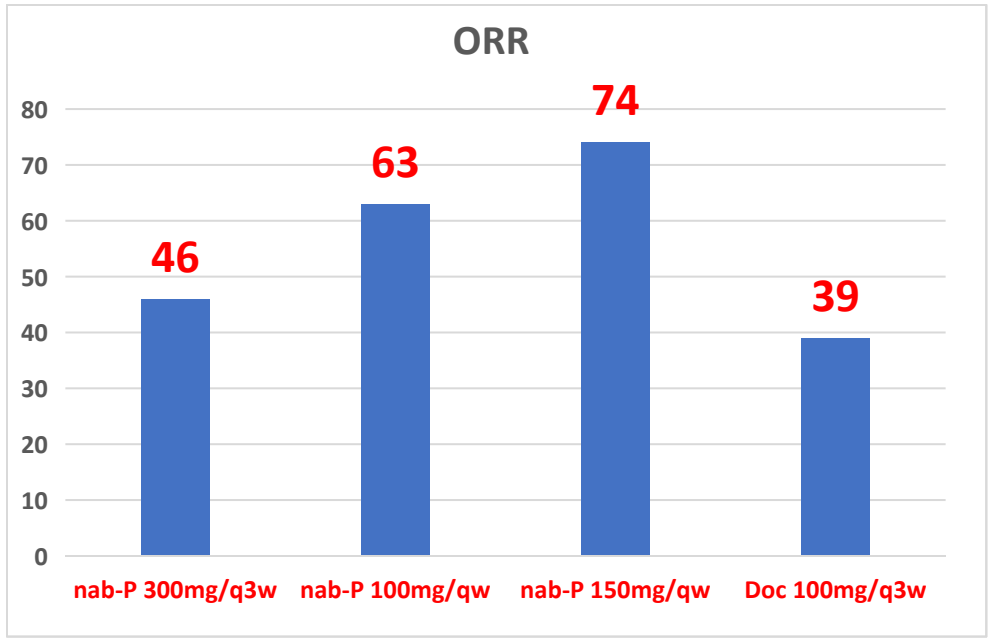
In this randomized, multicenter study, patients (N = 302) with previously untreated MBC received *nab*-paclitaxel 300 mg/m^2 q3w, 100 mg/m^2 weekly, or 150 mg/m^2 weekly or docetaxel 100 mg/m^2 q3w.

Table 2. Confirmed ORR and DCR

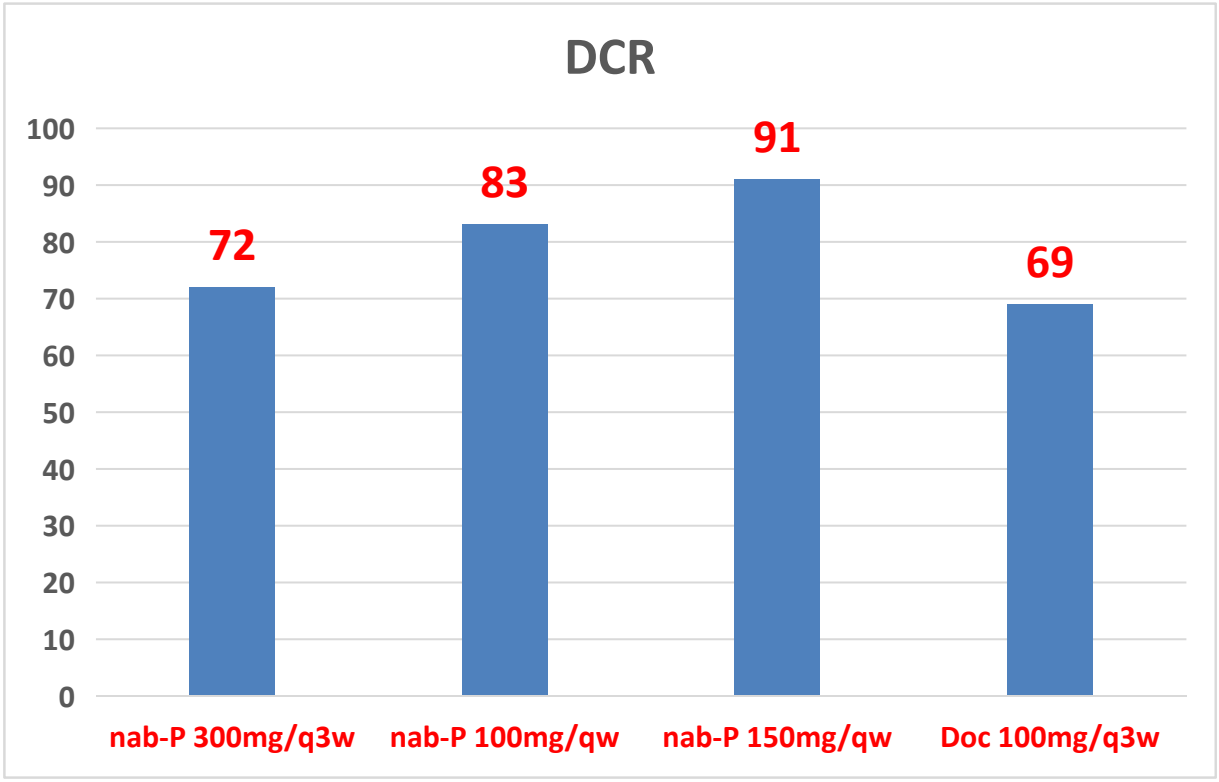
ORR and DCR	*nab*-Paclitaxel 300 mg/m^2 q3w (n = 76)	*nab*-Paclitaxel 100 mg/m^2 Weekly (n = 76)	*nab*-Paclitaxel 150 mg/m^2 Weekly (n = 74)	Docetaxel 100 mg/m^2 q3w (n = 74)	*P*
Investigator assessment					
Confirmed ORR					Overall: < .001; 150 mg/m^2 *v* D: < .001; 100 mg/m^2 *v* D: .002; 300 mg/m^2 *v* 150 mg/m^2: .002; 300 mg/m^2 *v* 100 mg/m^2: .024
No.	35	48	55	29	
%	46	63	74	39	
95% CI	34.8 to 57.3	52.3 to 74.0	64.4 to 84.3	28.1 to 50.3	
PR					
No.	34	46	53	27	
%	45	61	72	36	
CR					
No.	1	2	2	2	
%	1	3	3	3	
DCR					Overall: .007; 150 mg/m^2 *v* D: .005; 100 mg/m^2 *v* D: .009; 300 mg/m^2 *v* 150 mg/m^2: .014
No.	55	63	67	51	
%	72	83	91	69	
95% CI	62.3 to 82.4	74.4 to 91.4	83.9 to 97.2	58.4 to 79.5	
SD ≥ 16 weeks					
No.	20	15	12	22	
%	26	20	16	30	

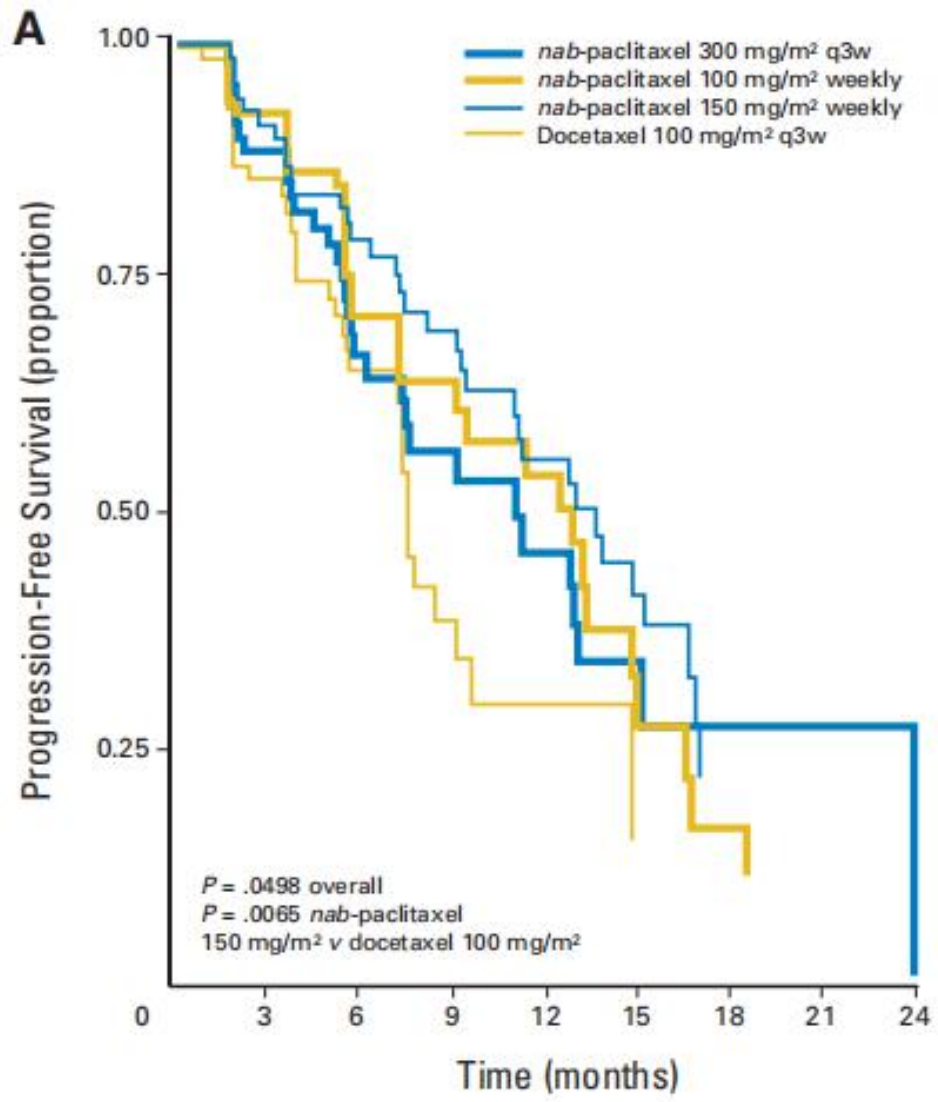
A. 白紫 300mg/M2 q3w
B. 白紫 100mg/M2 周疗
C. 白紫 150mg/M2 周疗
D. 多西他赛 100mg/M2 q3w

晚期研究 nab-Pa 与多西他赛 比较



17% 28%





化疗方案	中位*PFS(月)
A组: 白蛋白结合型紫杉醇 300mg/m²，q3w	11
B组: 白蛋白结合型紫杉醇 100mg/m²，qw，3/4	12.8
C组: 白蛋白结合型紫杉醇 150mg/m²，qw，3/4	12.9
D 组: 多西他赛 100mg/m²，q3w	7.5

Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negative breast cancer (IMpassion130): updated efficacy results from a randomised, double-blind, placebo-controlled, phase 3 trial

Peter Schmid, Hope S Rugo*, Sylvia Adams, Andreas Schneeweiss, Carlos H Barrios, Hiroji Iwata, Véronique Diéras, Volkmar Henschel, Luciana Molinero, Stephen Y Chui, Vidya Maiya, Amreen Husain, Eric P Winer, Sherene Loi, Leisha A Emens, for the IMpassion130 Investigators†*

IMpassion130 研究设计

IMpassion130主要入组条件 [a]:

- 转移性或不可手术的局部晚期TNBC
  - 组织病理学确认[b]
- 没有既往针对晚期TNBC的治疗
  - 既往辅助/新辅助治疗，包括紫杉烷，TFI（无治疗间期）≥ 12 个月
- ECOG PS 0-1

分层因素:

- 既往紫杉烷使用(是 vs 否)
- 肝转移(是 vs 否)
- 免疫细胞PD-L1状态 (阳性 [≥ 1%] vs 阴性 [< 1%])[c]

R 1:1

Atezo + 白蛋白紫杉醇:
阿替利珠单抗 840 mg IV
- On days 1 and 15 of 28-day cycle

+ *白蛋白紫杉醇* 100 mg/m² IV
- On days 1, 8 and 15 of 28-day cycle

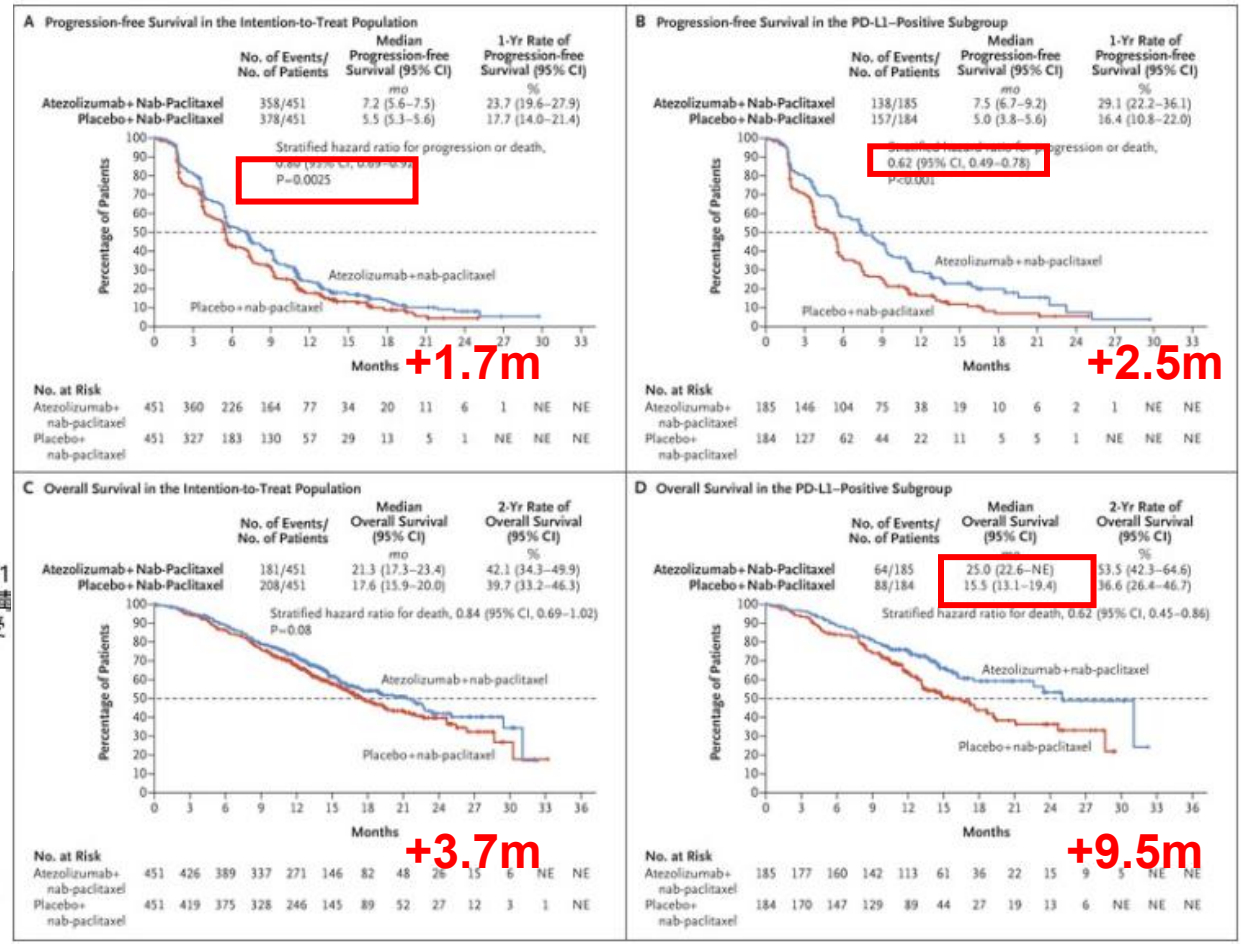
双盲; 不允许交叉

安慰剂+ 白蛋白紫杉醇:
安慰剂 IV
- On days 1 and 15 of 28-day cycle

+ *白蛋白紫杉醇* 100 mg/m² IV
- On days 1, 8 and 15 of 28-day cycle

RECIST v1.1 疾病进展或毒性不能耐受

- 共同主要研究终点：ITT和PD-L1+人群的PFS和OS [d]
  - 关键次要疗效研究终点（ORR 和 DOR）以及安全性评估



2019 年 3 月，Tecentriq 联合白紫用于 PD-L1 阳性转移性三阴性乳腺癌（TNBC）的适应症基于 IMpassion130 研究的 PFS 结果而获得加速批准。

IMpassion131

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

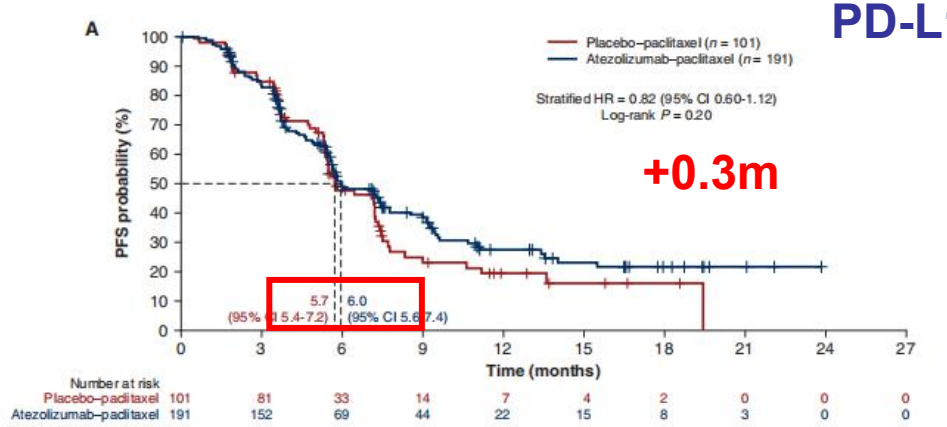
ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

paclitaxel 90 mg/m2 (days 1, 8, 15)

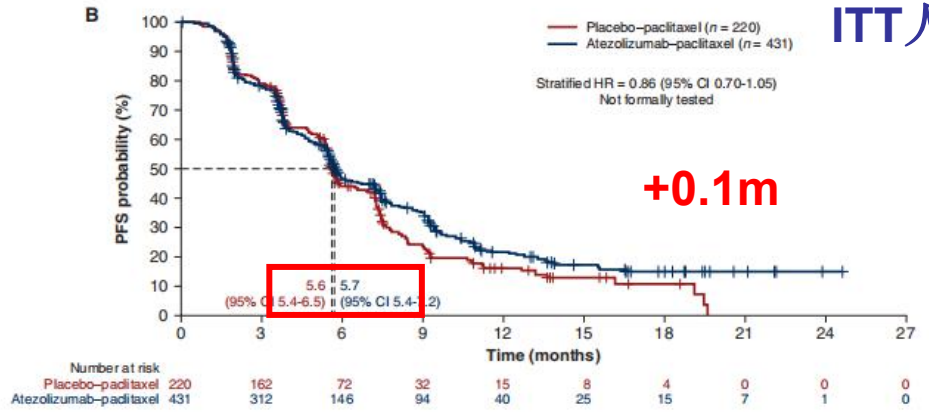
Primary results from IMpassion131, a double-blind, placebo-controlled, randomised phase III trial of first-line paclitaxel with or without atezolizumab for unresectable locally advanced/metastatic triple-negative breast cancer

PD-L1阳性

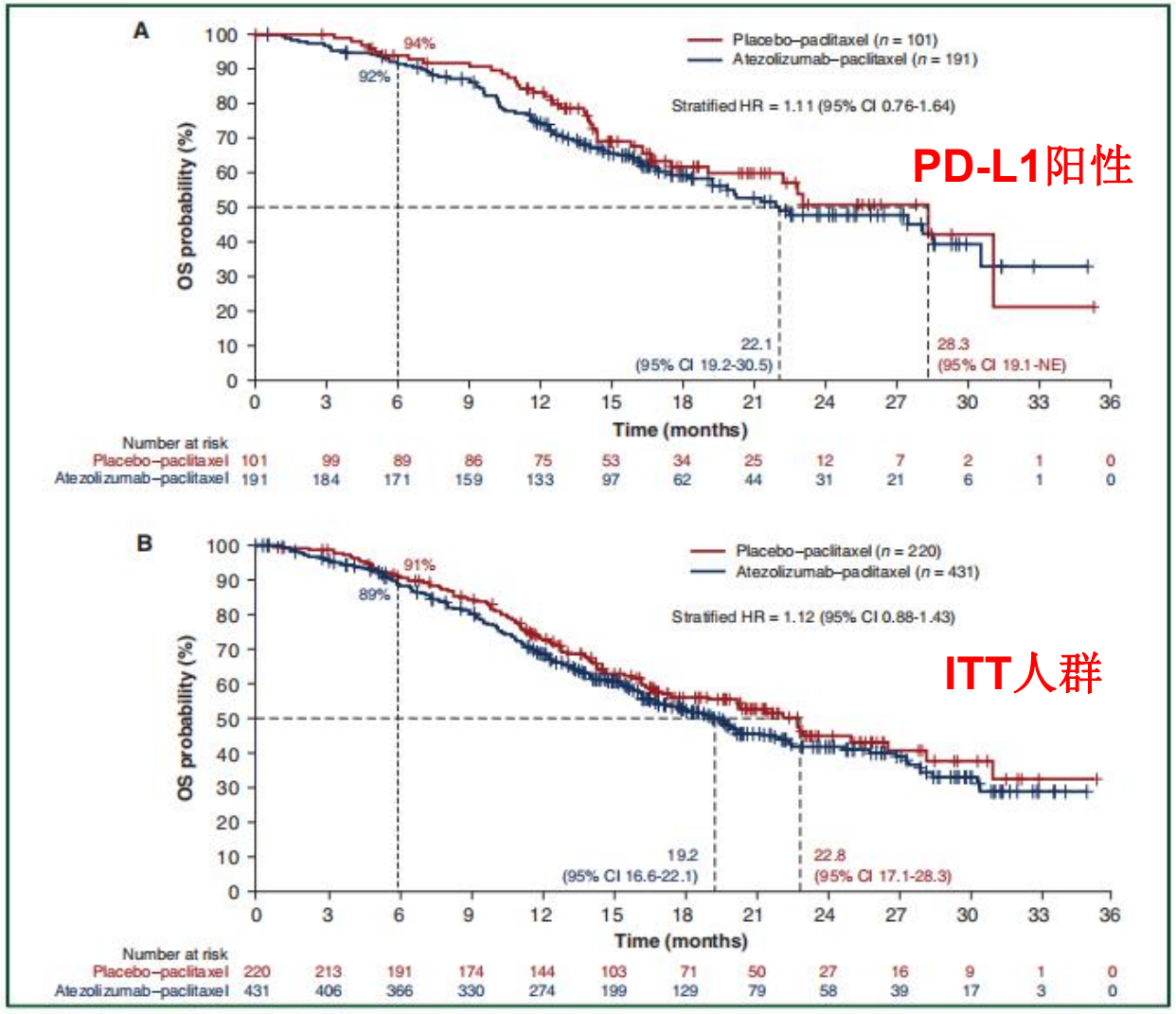


+0.3m

ITT人群



+0.1m



PD-L1阳性

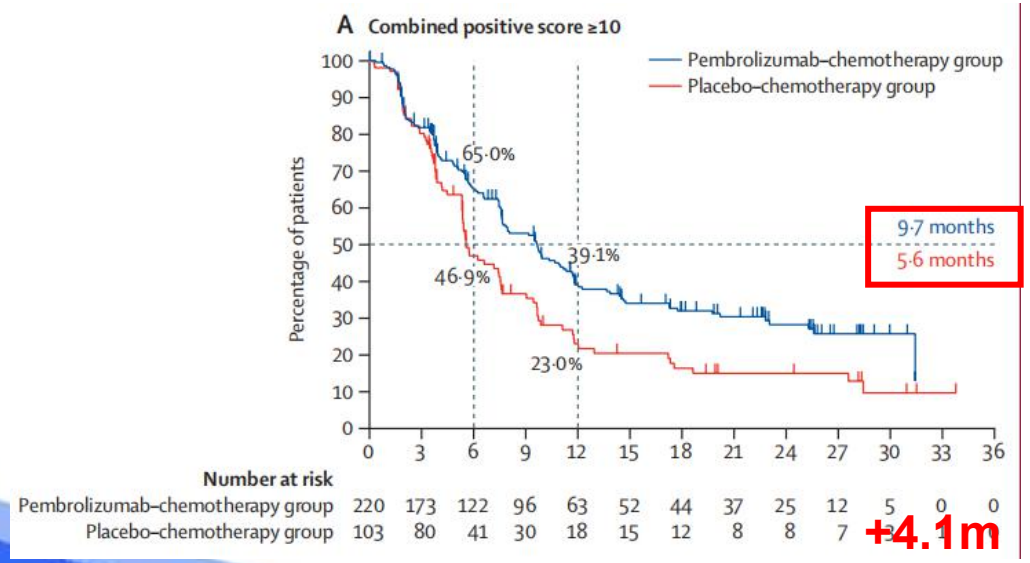
ITT人群

2021.08 Tecentriq 撤回三阴乳腺癌晚期一线适应症

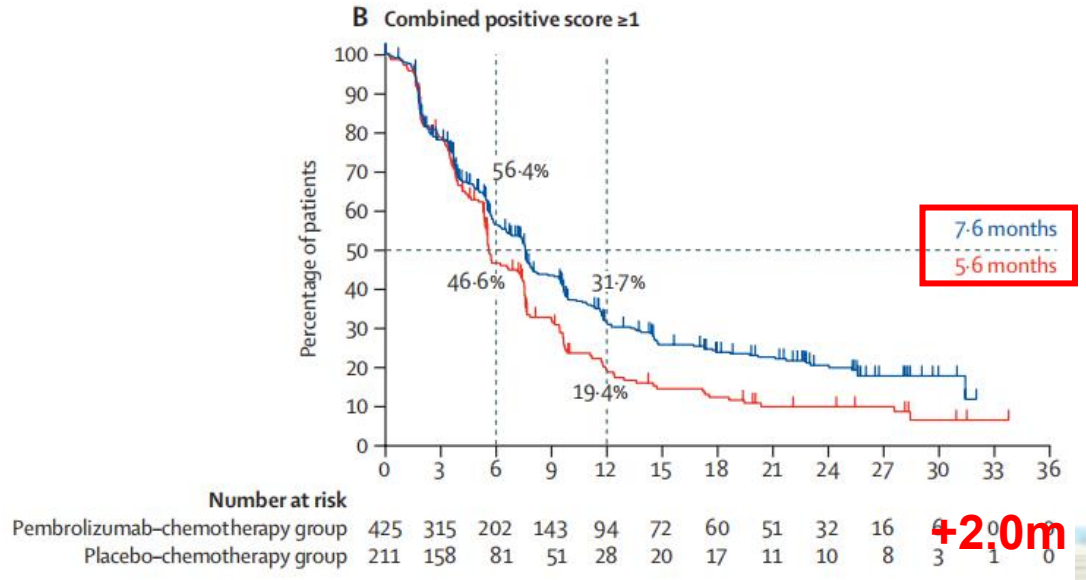
Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomised, placebo-controlled, double-blind, phase 3 clinical trial

KEYNOTE-355研究的主要疗效评估终点是两组PD-L1 CPS≥10、CPS≥1以及ITT人群PFS及OS

PFS



PFS



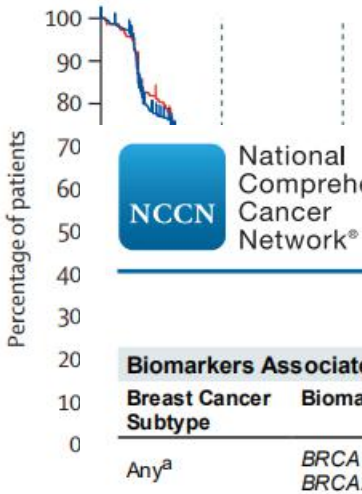
keynote 355

醫道從德 术業求精

+1.9m

PFS

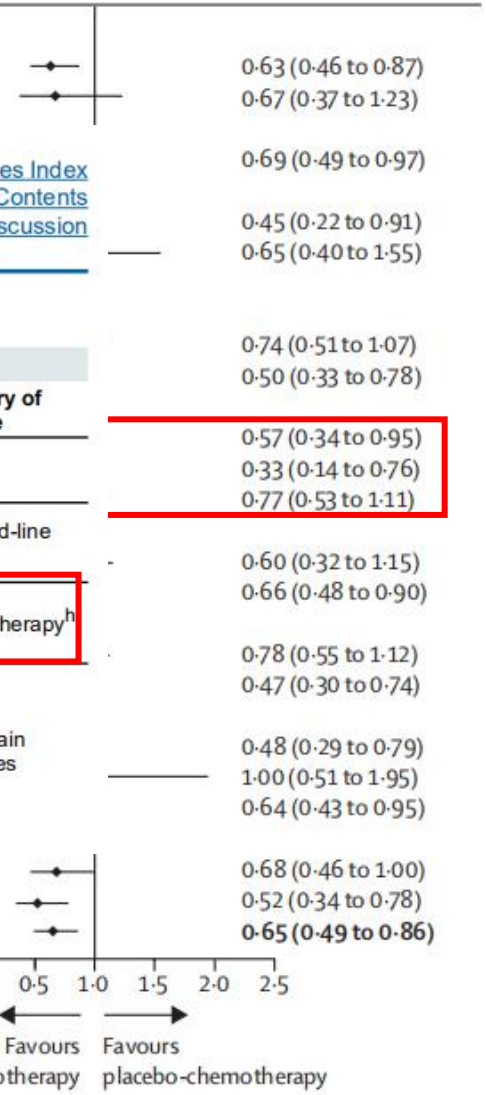
C Intention-to-treat population

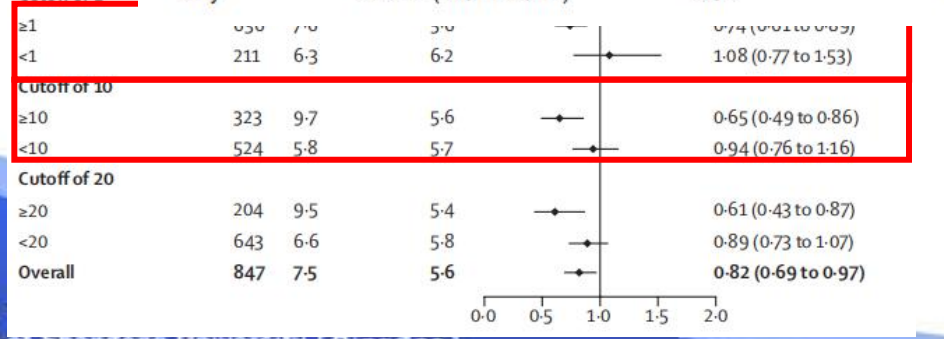


Number at risk
Pembrolizumab–chemotherapy group
Placebo–chemotherapy group

A PD-L1 comb

B Combined positive score ≥10





NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 8.2021
Invasive Breast Cancer

NCCN Guidelines Index
Table of Contents
Discussion

ADDITIONAL TARGETED THERAPIES AND ASSOCIATED BIOMARKER TESTING FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE

Biomarkers Associated with FDA-Approved Therapies

Breast Cancer Subtype	Biomarker	Detection	FDA-Approved Agents	NCCN Category of Evidence	NCCN Category of Preference
Any[a]	*BRCA1* mutation *BRCA2* mutation	Germline sequencing	Olaparib Talazoparib	Category 1 Category 1	Preferred
HR-positive/ HER2-negative[b]	*PIK3CA* activating mutation	PCR (blood or tissue block if blood negative), molecular panel testing	Alpelisib + fulvestrant[c]	Category 1	Preferred second-line therapy
TNBC	PD-L1 expression Threshold for positivity combined positive score ≥10	IHC	Pembrolizumab + chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine and carboplatin)[d]	Category 1	Preferred first-line therapy[h]
Any	*NTRK* fusion	FISH, NGS, PCR (tissue block)	Larotrectinib[e] Entrectinib[e]	Category 2A	Useful in certain circumstances
Any	MSI-H/dMMR	IHC, PCR (tissue block)	Pembrolizumab[d,f] Dostarlimab-gxly[g]	Category 2A	
Any	TMB-H (≥10 muts/mb)	NGS	Pembrolizumab[d,f]	Category 2A	

目录

5.6 Ⅳ期无驱动基因非鳞癌非小细胞肺癌的治疗

分期	分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
Ⅳ期无驱动基因、非鳞癌NSCLC一线治疗[a]	PS=0~1	1. 培美曲塞联合铂类+培美曲塞单药维持治疗 2. 贝伐珠单抗[b]联合含铂双药化疗[1,2]+贝伐珠单抗维持治疗 3. 含顺铂或卡铂双药方案：顺铂/卡铂联合吉西他滨或多西他赛或紫杉醇或紫杉醇脂质体（2A类）或长春瑞滨或培美曲塞 4. 阿替利珠单抗［限PD-L1 TC≥50%或IC≥10%］[3] 5. 帕博利珠单抗单药（限PD-L1 TPS≥50%，PD-L1 TPS 1%~49%（2A类））[4,5]； 6. 培美曲塞+铂类联合帕博利珠或卡瑞利珠或信迪利或替雷利珠单抗[6-9]	1. 紫杉醇+卡铂+贝伐珠单抗联合阿替利珠单抗[10] 2. 白蛋白紫杉醇+卡铂联合阿替利珠单抗[11] 3. 重组人血管内皮抑制素联合长春瑞滨和顺铂+重组人血管内皮抑制素维持治疗（2B类）	纳武利尤单抗[illegible]联合两周期培美曲塞+铂类[12]

Impower150

Impower130

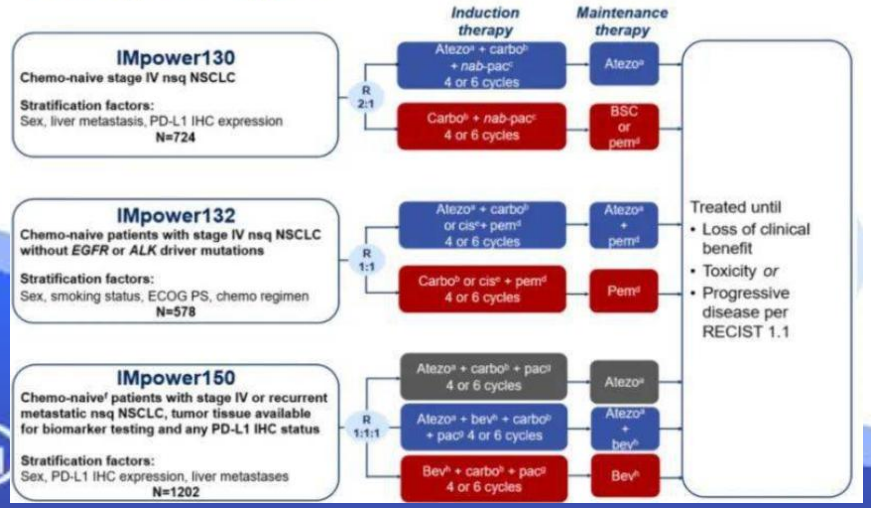
Ⅳ期无驱动基因鳞癌的治疗

分期	分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
Ⅳ期无驱动基因、鳞癌一线治疗[a]	PS=0~1	1. 含顺铂或卡铂双药方案：顺铂/卡铂联合吉西他滨或多西他赛或紫杉醇或脂质体紫杉醇 2. 含奈达铂双药方案：奈达铂+多西他赛（1B类）[1] 3. 阿替利珠单抗［限PD-L1 TC≥50%或IC≥10%］[2] 4. 帕博利珠单抗单药（限PD-L1 TPS≥50%，PD-L1TPS1%~49%(2A类)）[3,4]； 5. 紫杉醇/白蛋白紫杉醇+铂类联合帕博利珠或替雷利珠单抗[5,6] 6. 吉西他滨+铂类联合信迪利单抗[7]	紫杉醇+铂类联合卡瑞利珠单抗[8]	1. 白蛋白紫杉醇+卡铂（2B类）[9] 2. 纳武利尤单抗和伊匹木单抗联合两周期紫杉醇+铂类[10]

keynote 407

RATIONALE 307

Study designs



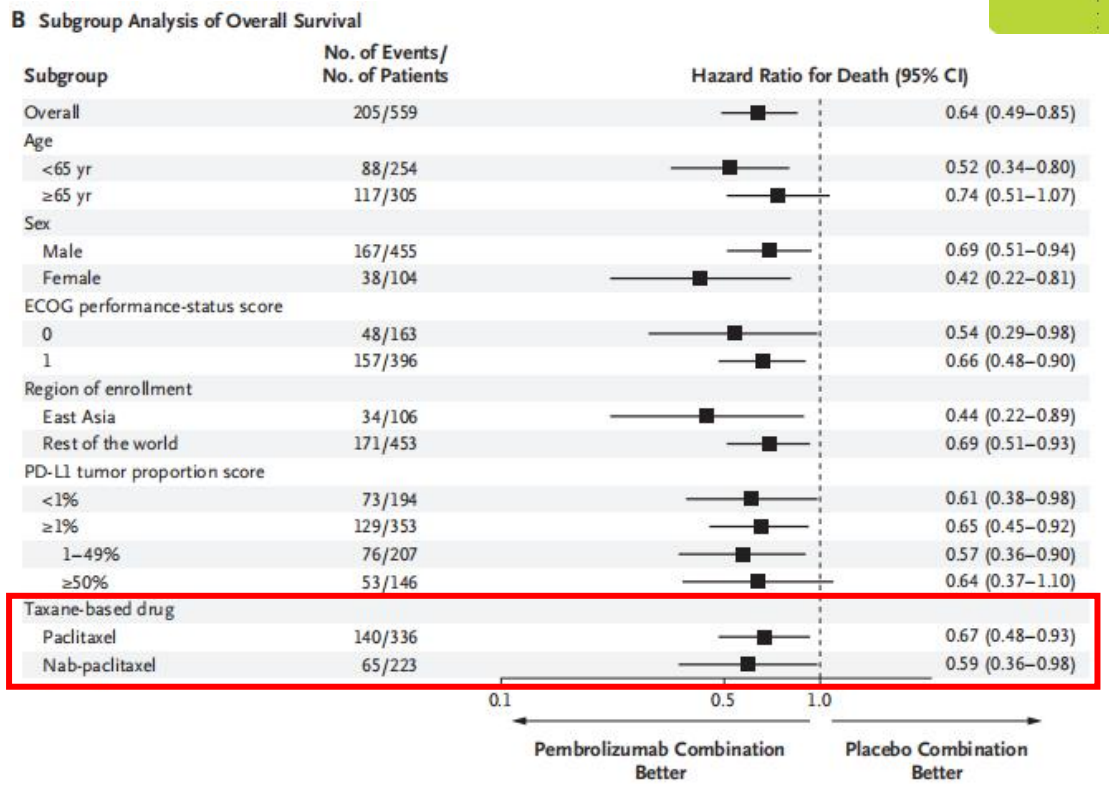
nab-PP 方案	白蛋白紫杉醇	100mg/m^2	d1，8，15
	顺铂或卡铂		

21d

keynote 407

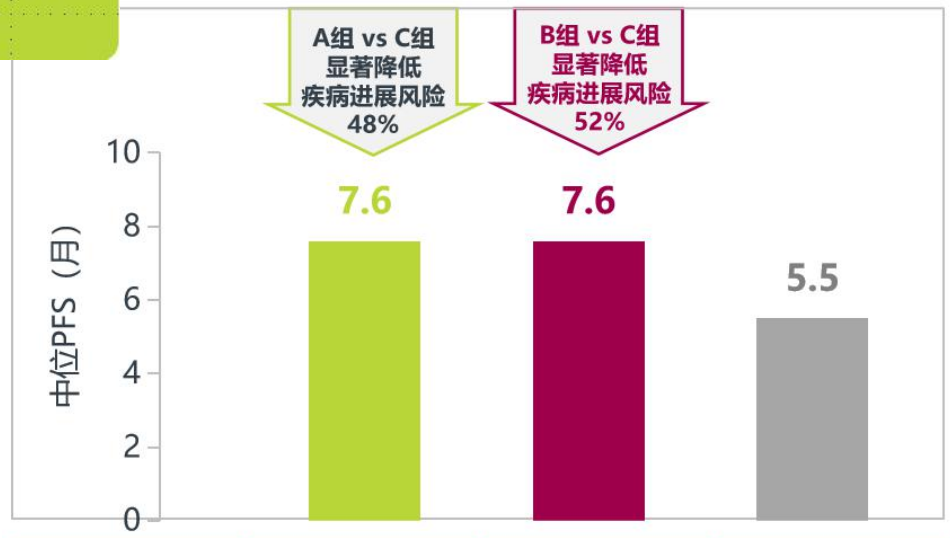
Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer

B Subgroup Analysis of Overall Survival



帕博利珠单抗 200mg Q3w
卡铂 AUC6 Q3w
+紫杉醇 200mg /m² Q3w或白蛋白结合型紫杉醇100 mg/m² Qw
X4周期(每3w)

RATIONALE 307



	A组 替雷利珠单抗+紫杉醇+卡铂 (n=120)	B组 替雷利珠单抗+白紫+卡铂 (n=119)	C组 紫杉醇+卡铂 (n=121)
中位PFS, 月 (95% CI)	7.6(6.0-9.8)	7.6(5.8-11.0)	5.5 (4.2-5.7)
HR (95% CI)	0.52(0.4-0.7)	0.48(0.3-0.7)	NA
P值	0.0001	<0.0001	

免疫+Nab-pa较免疫+紫杉醇更降低死亡及疾病进展风险。

SCIENTIFIC REPORTS

Nab-Paclitaxel in combination with Cisplatin Versus Docetaxel Plus Cisplatin as First-Line Therapy in Non-small Cell Lung Cancer

纳入标准：
- **n=271**
- 年龄≥18岁（中位年龄：58岁）
- 组织学或细胞学证实：无法手术切除的晚期NSCLC（IIIB/IV期）
- 至少1个可测量病灶
- 既往未接受化疗，但允许进行辅助或新辅助治疗；不能同时进行免疫治疗；无其他肿瘤
- ECOG评分：0-1

nab-PTX+顺铂（n=55）：
- nab-PTX（130 mg/m²，d1，8）
- 顺铂（75 mg/m²，d1）
- 3周 / 周期

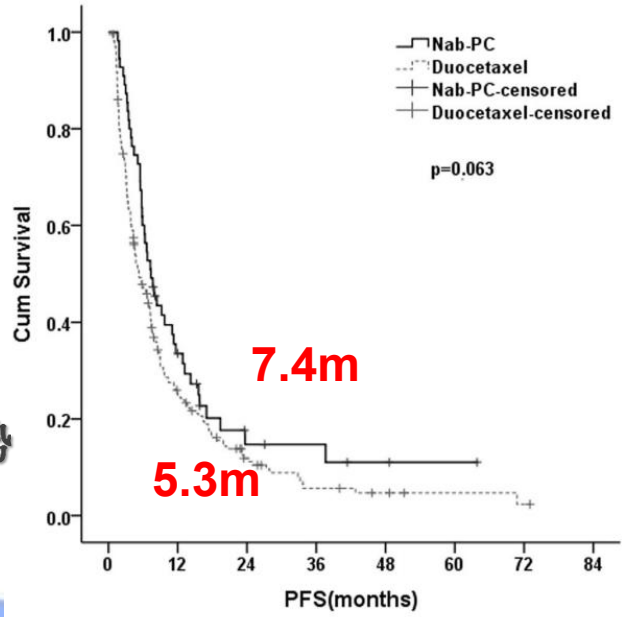
多西他赛+顺铂（n=216）：
- 多西他赛（75mg/m²，d1）
- 顺铂（75 mg/m²，d1）
- 3周 / 周期

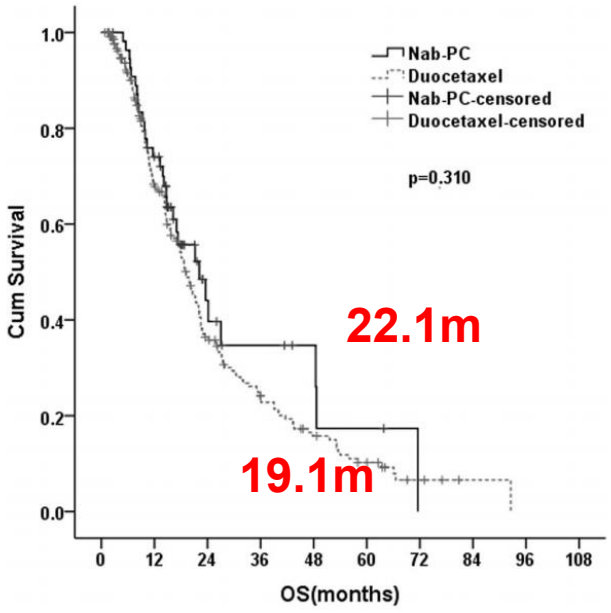
主要终点：
- ORR

次要终点：
- DCR
- PFS
- OS

安全性终点：
- 治疗相关不良事件

Response rates	Nab-PC(N = 55) No.(%)	Decetaxel(N = 216) No.(%)
Total population		
Overall response	26(47.3%)	69(31.9%)
Complete response	2(3.6%)	1(0.5%)
Partial response	24(43.6%)	68(31.5%)
Stable disease	23(41.8%)	70(32.4%)
Progressive disease	6(10.9%)	77(35.6%)
Squamous Subset	n = 24	n = 93
Overall response	14(58.3%)	27(29.0%)
Nonsquamous Subset	n = 31	n = 123
Overall response	12(38.7%)	42(34.1%)





延长趋势

Nab-Pa维持治疗 ABOUND研究

Clin Lung Cancer. 2021 Jan;22(1):6-15.e4. doi: 10.1016/j.cllc.2020.09.007. Epub 2020 Sep 18.

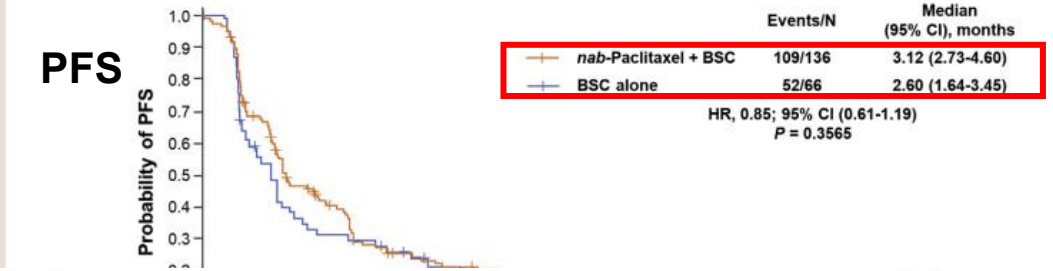
Nanoparticle Albumin-bound Paclitaxel Plus Carboplatin Induction Followed by Nanoparticle Albumin-bound Paclitaxel Maintenance in Squamous Non-Small-ce Cancer (ABOUND.sqm): A Phase III Randomized Clinical Trial

Abstract

Prospective randomized studies of maintenance therapy for patients with squamous non–small-cell lung cancer are lacking. In the present study, patients without disease progression after induction treatment were randomized 2:1 to maintenance nanoparticle albumin-bound paclitaxel plus best supportive care or best supportive care alone. The primary endpoint (progression-free survival) was not met. Given the current treatment paradigm, these findings can be expected to minimally affect treatment practice.

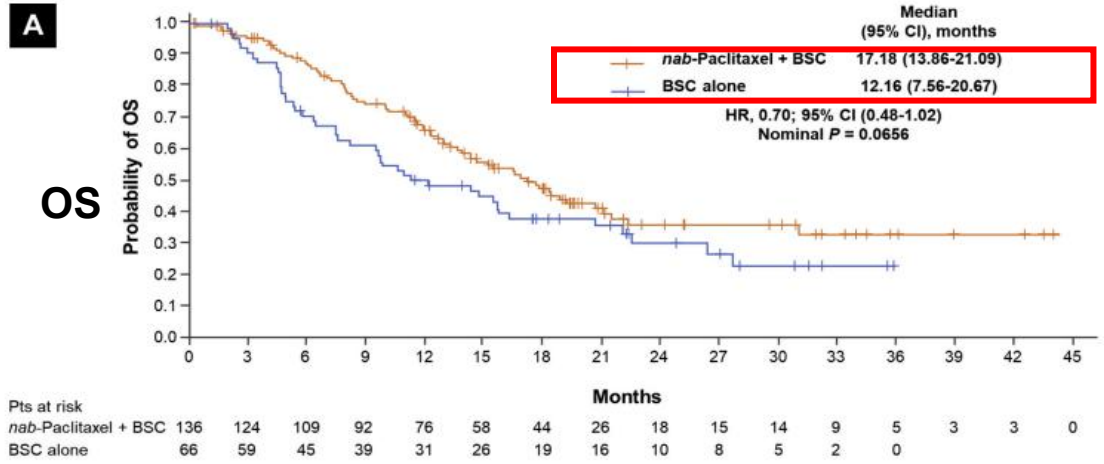
Background: We evaluated maintenance nanoparticle albumin-bound (nab) paclitaxel in the treatment of advanced squamous non–small-cell lung cancer. **Patients and Methods:** Patients with treatment-naive squamous non–small-cell lung cancer received four 21-day cycles of nab-paclitaxel 100 mg/m^2 on days 1, 8, 15 plus carboplatin area under the curve 6 on day 1 as induction therapy. Patients without disease progression after induction were randomized 2:1 to maintenance nab-paclitaxel 100 mg/m^2 (days 1 and 8 every 21 days) plus best supportive care (BSC) or BSC alone. The primary endpoint was progression-free survival (PFS). Secondary endpoints included safety and overall survival (OS). **Results:** Overall, 420 patients had received induction therapy; 202 (nab-paclitaxel plus BSC, 136; BSC, 66) had received maintenance therapy. Enrollment was discontinued after a preplanned interim futility analysis (patients could remain in the study at the investigator's discretion). The median PFS was 3.12 months for nab-paclitaxel plus BSC and 2.60 months for BSC; the difference was not statistically significant (hazard ratio [HR], 0.85; 95% confidence interval [CI], 0.61-1.19; $P = .36$). The median OS (median follow-up, 24.2 months) was 17.18 months for nab-paclitaxel plus BSC and 12.16 months for BSC (HR, 0.70; 95% CI, 0.48-1.02; nominal $P = .07$). An updated analysis (median follow-up, 28.4 months) revealed a median OS of 17.61 months for nab-paclitaxel plus BSC and 12.16 months for BSC (HR, 0.68; 95% CI, 0.47-0.98; nominal $P = .037$). The most frequent grade 3 and 4 treatment-emergent adverse events for the entire study were neutropenia (53.1% [nab-paclitaxel plus BSC] vs. 50.0% [BSC]) and anemia (33.1% [nab-paclitaxel plus BSC] vs. 32.3% [BSC]). Only peripheral neuropathy had occurred in ≥ 5% of patients during maintenance therapy (13.1%; nab-paclitaxel plus BSC). **Conclusions:** The results of the ABOUND.sqm did not meet the primary endpoint of PFS. An updated OS analysis revealed a trend favoring nab-paclitaxel plus BSC.

PFS

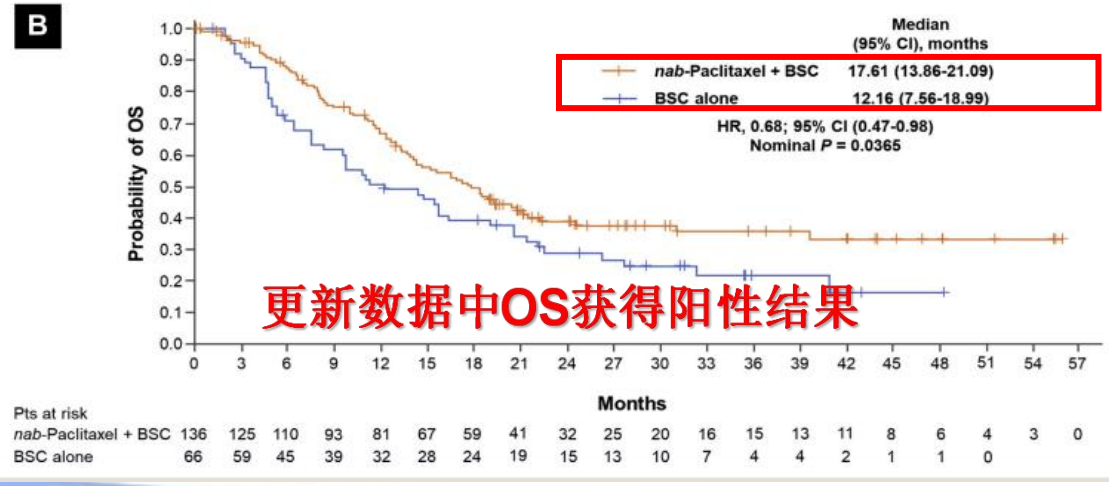


OS

A



B



更新数据中OS获得阳性结果

（一）小细胞肺癌的二线治疗

分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
≤ 6 个月复发	拓扑替康（1 类）[1-3] 参加临床试验	伊立替康（2A 类）[4] 紫杉醇（2A 类）[5, 6] 多西他赛（2A 类）[7] 吉西他滨（2A 类）[口服依托泊苷（2A 长春瑞滨（2A 类）[替莫唑胺（2A 类）[	苯达莫司汀（2B 类）[16]
>6 个月复发	选用原方案 *		

*. 不适用于一线应用免疫靶向药物治疗的患者，对于使用 atezol
复发的患者，建议再次使用卡铂 + 依托泊苷或顺铂 + 依托泊苷。

PRINCIPLES OF SYSTEMIC THERAPY

SCLC SUBSEQUENT SYSTEMIC THERAPY (PS 0–2)[c]
Consider dose reduction or growth factor support for patients with PS 2.

Relapse ≤6 months	Relapse >6 months
Preferred Regimens • Topotecan PO or IV[14-16] • Lurbinectedin[17] • Clinical trial **Other Recommended Regimens** • Paclitaxel[18,19] • Docetaxel[20] • Irinotecan[21] • Temozolomide[22,23] • Cyclophosphamide/doxorubicin/vincristine (CAV)[14] • Oral etoposide[24,25] • Vinorelbine[26,27] • Gemcitabine[28,29] • Nivolumab[b,d,30,31] • Pembrolizumab[b,d,32-34] • Bendamustine (category 2B)[35]	**Preferred Regimens** • Original regimen[d,36,37] **Other Recommended Regimens** • Topotecan PO or IV[14-16] • Paclitaxel[18,19] • Docetaxel[20] • Irinotecan[21] • Temozolomide[22,23] • CAV[14] • Oral etoposide[24,25] • Vinorelbine[26,27] • Gemcitabine[28,29] • Nivolumab[b,d,30,31] • Pembrolizumab[b,d,32-34] • Lurbinectedin[38] • Bendamustine (category 2B)[35]

Mol Clin Oncol. 2016 Jul;5(1):213-215. doi: 10.3892/mco.2016.887. Epub 2016 May 6.

Albumin-bound paclitaxel for the treatment of refractory or relap cancer

Abstract. Since nanoparticle albumin-bound (nab)-paclitaxel exerts clinically meaningful antitumor effects on various malignancies, including breast, gastric and non-small-cell lung cancer, we hypothesized that treatment with nab-paclitaxel may also be beneficial for patients with small-cell lung cancer (SCLC). We herein evaluated the safety and efficacy of weekly, single-agent nab-paclitaxel in patients with refractory or relapsed SCLC. Between May, 2013 and February, 2015, 9 patients with refractory or relapsed SCLC were treated with single-agent nab-paclitaxel at the Kyoto University Hospital. The medical records of the patients were retrospectively reviewed. All the patients had been previously treated with ≥2 lines of chemotherapy prior to receiving nab-paclitaxel. The median number of cycles of nab-paclitaxel was 2 (range, 1-4) and 3 partial responses were observed (response rate: 33%). The toxicity was generally mild and manageable: Grade 3/4 adverse events were only observed in 1 patient (grade 3 leukopenia). Thus, weekly administration of nab-paclitaxel may be a viable treatment option in patients with refractory or relapsed SCLC. Considering that treatment options are quite limited in this patient population, further evaluation of this regimen may prove valuable in the clinical setting.

Medicine®

Observational Study

OPEN

Efficacy of nanoparticle albumin-bound paclitaxel regimens for relapsed small cell lung cancer

A retrospective analysis

The response rates, disease control rates, and median overall survival for the total patient population were 36%, 64%, and 7.8 months, respectively. Response rates, disease control rates, and the median overall survival were 11%, 44%, and 4 months, respectively, in the monotherapy group; and 80%, 100%, and 10.6 months, respectively, in the combination therapy group. The most common adverse events were hematological toxicities such as neutropenia and anemia. Severe neutropenia appeared in some patients, although it was resolved by treatment in all. The most common nonhematological toxicity was anorexia (64%), followed by neurotoxicity and constipation. All nonhematological toxicities were mild and manageable.

Our results suggest that chemotherapy with nab-paclitaxel regimens for relapsed SCLC exhibits moderate clinical efficacy and is well-tolerated. Further clinical trials in relapsed SCLC patients are warranted.

	ORR	DCR	PFS	OS
nab-PTX	11%	44%	2.0	4.0
nab-PTX+卡铂	80%	100%	3.6	10.6
总体人群	36%	64%	2.9	7.8

We retrospectively surveyed the databases at the 2 hospitals and enrolled 14 patients with histologically and cytologically confirmed SCLC who were treated with nab-paclitaxel regimens

目录

术后治疗方案：

紫杉醇＋顺铂（仅对食管鳞癌）[10]

紫杉醇 150mg/m^2 i.v. d1

顺铂 50mg/m^2 i.v. d1

每 2 周重复

远处转移性食管癌的治疗原则

一线治疗

分层		Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
HER-2 阳性腺癌	PS ≤ 2	曲妥珠单抗联合氟尿嘧啶＋顺铂（1A 类）		曲妥珠单抗联合其他一线化疗方案（2B 类）
鳞癌、HER-2 阴性腺癌	PS=0~2	氟尿嘧啶＋顺铂（鳞癌，2A 类） 氟尿嘧啶类（5-FU 或卡培他滨或替吉奥）＋顺铂（腺癌，1A 类）	帕博利珠单抗＋氟尿嘧啶类（5-FU 或卡培他滨）＋顺铂（CPS ≥ 10，1A 类） 卡瑞利珠单抗＋紫杉醇＋顺铂（鳞癌，1A 类）	白蛋白结合型紫杉醇＋顺铂（鳞癌，3 类） 卡瑞利珠单抗＋阿帕替尼＋紫杉醇脂质体＋奈达铂（鳞癌，3 类）

二线及以上治疗

分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
PS=0-2	卡瑞利珠单抗（鳞癌，1A 类） 帕博利珠单抗（鳞癌，PD-L1 CPS ≥ 10，1A 类） 氟尿嘧啶＋伊立替康（腺癌，2A 类） 伊立替康＋替吉奥（鳞癌，2A 类） HER-2 阳性腺癌，如果铂类治疗失败且既往未应用过曲妥珠单抗，则建议曲妥珠单抗联合紫杉醇（1A/2A 类） 多西他赛单药（腺癌，1A 类） 紫杉醇单药（腺癌，1A 类） 伊立替康单药（腺癌，1A 类）	纳武利尤单抗（鳞癌，1A 类） 安罗替尼[a]（鳞癌，2A 类） 多西他赛单药（鳞癌，3 类） 紫杉醇单药（鳞癌，3 类） 伊立替康单药（鳞癌，3 类） 阿帕替尼（腺癌，1A 类）（鳞癌，3 类）	白蛋白结合型紫杉醇单药（鳞癌，3 类） 卡瑞利珠单抗＋阿帕替尼（鳞癌，3 类）
PS ≥ 3	最佳支持治疗 / 对症处理（2A 类） 参加临床研究		

Onco Targets Ther.2016 Sep 23;9:5663-5669. doi: 10.2147/OTT.S108580. eCollection 2016.

Weekly nanoparticle albumin-bound paclitaxel in combination with cisplatin versus weekly solvent-based paclitaxel plus cisplatin as first-line therapy in Chinese patients with advanced esophageal squamous cell carcinoma

回顾性研究：

- ≥18岁
- 病理学或细胞学确诊的不可手术转移性食管鳞癌
- ECOG体能评分0-2
- 预计寿命 > 3个月
- 初治患者*
- 充分的骨髓和肝肾功能

nab-TP组 N=32
白紫 :125 mg/m² IV，d1、8
顺铂:75 mg/m² IV ,d1
21天一个周期

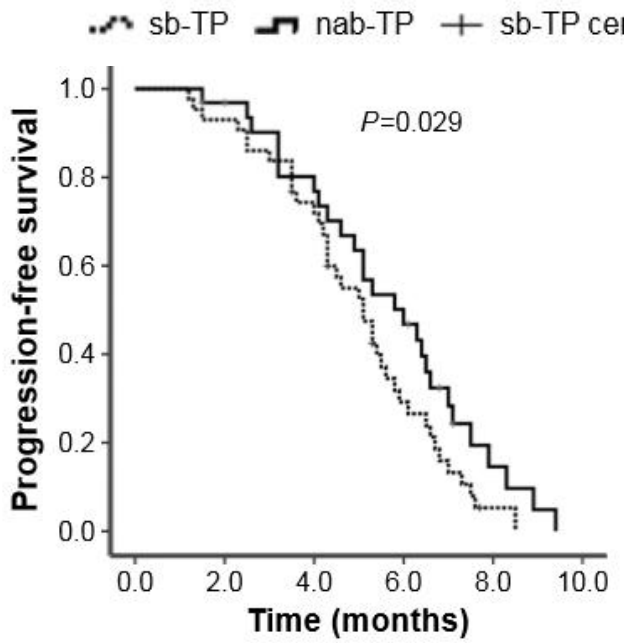
sb-TP组 N=43
紫杉醇**:80 mg/m² IV，d1、8
顺铂: 75 mg/m² IV，d1
21天一个周期

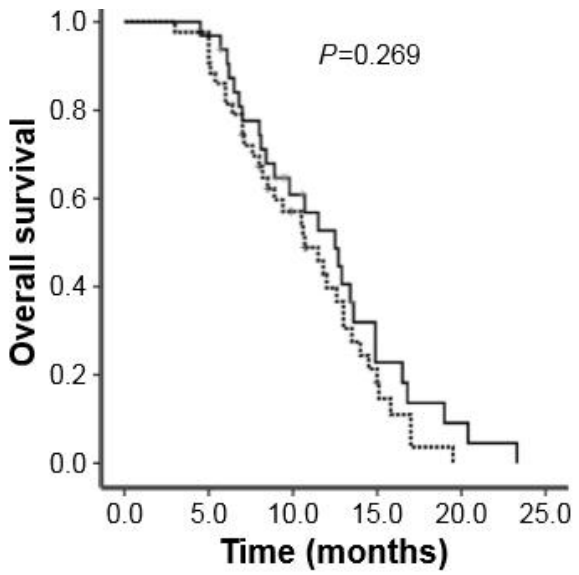
最多6-8周期
除非疾病进展
或不可耐受毒性

治疗期间每两周期
进行疗效评估
6-8周期后每12周
进行评估

主要评价：ORR、DCR、PFS、OS

肿瘤缓解	Nab-TP组 N=32	Sb-TP组 N=43	P值
CR	1（3%）	1（2%）	
PR	15（47%）	12（28%）	
SD	10（31%）	15（35%）	
PD	6（19%）	15（35%）	
ORR	**16（50%）**	**13（30%）**	**0.082**
DCR	26（81%）	28（65%）	0.124





中位PFS：Nab-TP：6.1 （5.5-7.1）
Sb-TP：5.0（4.1-6.1）

中位OS：Nab-TP：12.5 （9.4-15.6）
Sb-TP：10.7（8.1-13.3）

目录

2.1.1.2.3.2 新辅助治疗

治疗方式	分层*	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
新辅助治疗[e]	非食管胃结合部癌：cT3-4aN+M0，c Ⅲ期	新辅助化疗 SOX（1A 类）	新辅助化疗：DOS（1B 类）FLOT4（1B 类）	新辅助化疗：XELOX（2A 类）FLOFOX（2A 类）
	食管胃结合部癌[e, f]：cT3-4aN+M0，c Ⅲ期	新辅助放化疗：DT 45~50.4Gy（同期氟尿嘧啶类、铂类或紫杉类）（1B类）	新辅助化疗：XELOX（2A 类）FOLFOX（2A 类）SOX（1B 类）FLOT4（1B 类）DOS（1B 类）	新辅助放疗（不能耐受化疗者）（2B 类）

一线治疗

	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
HER2 阳性[i, j]	曲妥珠单抗联合奥沙利铂 / 顺铂 +5-FU/ 卡培他滨（1A 类）	曲妥珠单抗联合奥沙利铂 / 顺铂 + 替吉奥（2B 类）	曲妥珠单抗联合其他一线化疗方案（含蒽环类药物方案除外）（3 类）
Her2 阴性	奥沙利铂 + 氟尿嘧啶类（5-FU/ 卡培他滨 / 吉奥）（1A 类）	三药联合方案 DCF 及 mDCF（1B 类），适用于体力状况好且肿瘤负荷较大的患者	
	紫杉醇 / 多西紫杉醇 + 氟尿嘧啶类（5-FU/ 卡培他滨 / 替吉奥）（2A 类）		
	顺铂 + 氟尿嘧啶类（5-FU/ 卡培他滨 / 替吉奥）（1A 类）		
	PD-L1CPS ≥ 5，化疗（FOLFOX/XELOX）联合纳武利尤单抗（1A 类）。		PD-L1CPS ≥ 1，帕博利珠单抗单药

二线治疗 g

	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
Her2 阳性	单药化疗（紫杉醇 / 多西他赛 / 伊立替康）（1A 类）	如既往铂类治疗失败且未接受过曲妥珠单抗，曲妥珠单抗联合单药紫杉醇（2A 类）	如既往未应过曲妥珠单抗，曲妥珠单抗联合蒽环类之外的其他二线化疗方案（3 类）参考 HER2 阴性胃癌的二线治疗化疗药物选择鼓励参加临床研究
Her2 阴性	单药化疗（紫杉醇 / 多西他赛 / 伊立替康）（1A 类）	两药化疗，根据既往用药情况推荐伊立替康 + 5-FU，紫杉醇 / 多西紫杉醇 + 氟尿嘧啶类（5-FU/ 卡培他滨 / 替吉奥）（2B 类）白蛋白紫杉醇单药化疗（1B 类）MSI-H 人群中，帕博利珠单抗（2A 类）	如既往未经铂类治疗失败，顺铂或奥沙利铂为基础的化疗（3 类）

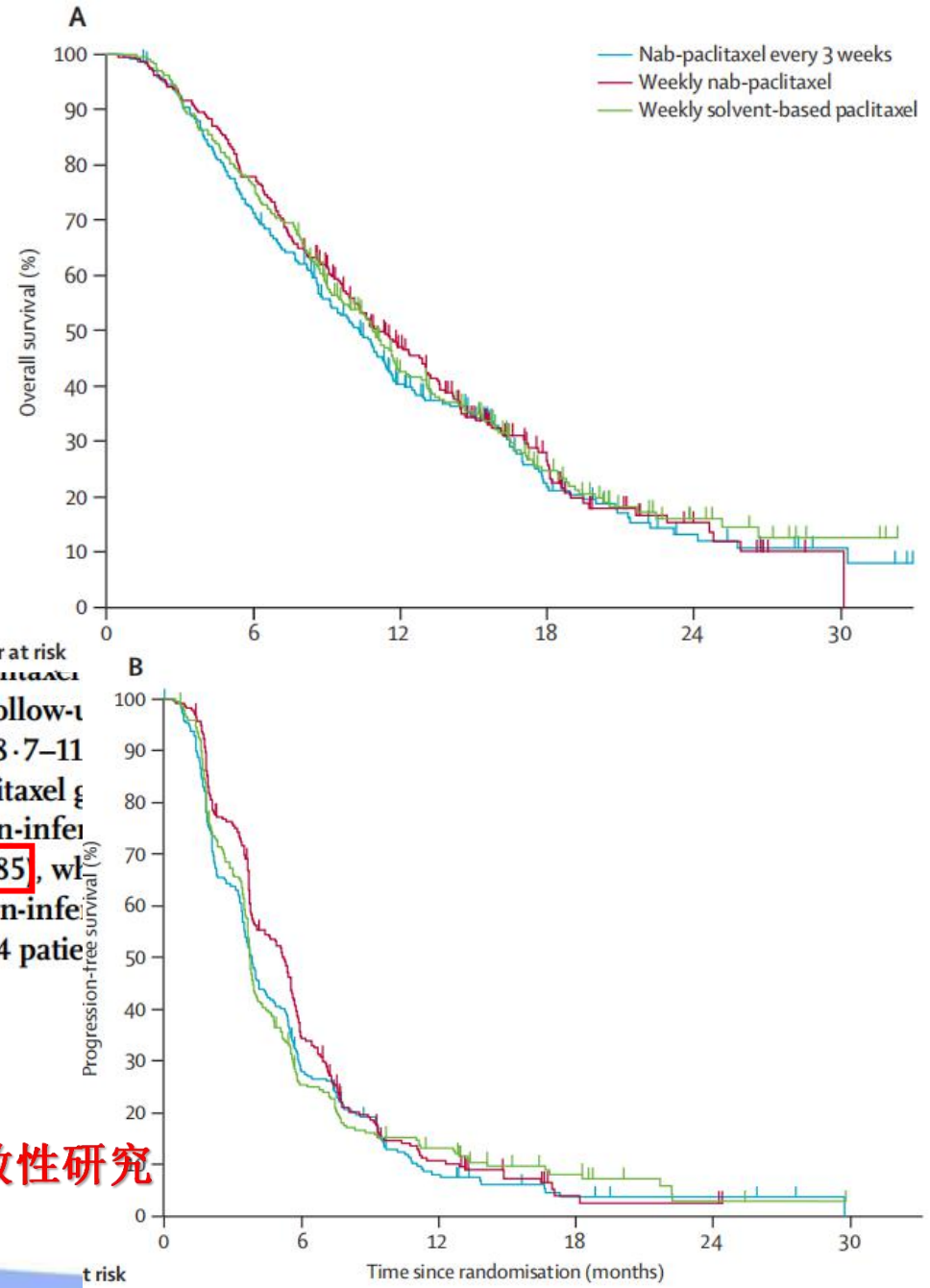
ABSOLUTE研究（日本III期）

Nab-paclitaxel versus solvent-based paclitaxel in patients with previously treated advanced gastric cancer (ABSOLUTE): an open-label, randomised, non-inferiority, phase 3 trial

Kohei Shitara, Atsuo Takashima, Kazumasa Fujitani, Keisuke Koeda, Hiroki Hara, Norisuke Nakayama, Shuichi Hironaka, Kazuhiro Nishikawa, Yoichi Makari, Kenji Amagai, Shinya Ueda, Kazuhiro Yoshida, Hideki Shimodaira, Tomohiro Nishina, Masahiro Tsuda, Yukinori Kurokawa, Takao Tamura, Yasutsuna Sasaki, Satoshi Morita, Wasaburo Koizumi

Methods We did a randomised, open-label, non-inferiority, phase 3 trial at 72 institutions in Japan. I 20 years or older with advanced gastric adenocarcinoma refractory to a fluoropyrimidine-contain chemotherapy regimen, with progressive disease or a relapse fewer than 24 weeks after the final dos chemotherapy were randomly assigned (1:1:1) to receive intravenous nab-paclitaxel (260 mg/m²) ev (on day 1 of a 21-day cycle), weekly nab-paclitaxel (100 mg/m², on days 1, 8, and 15 of a 28-day cycl solvent-based paclitaxel (80 mg/m², on days 1, 8, and 15 of a 28-day cycle). Randomisation was d minimisation method, with stratification for previous use of docetaxel, presence of peritoneal metastases

Findings Between March 13, 2013, and May 14, 2015, 741 patients were randomly assigned to nab-pac 3 weeks (n=247), weekly nab-paclitaxel (n=246), or weekly solvent-based paclitaxel (n=248). Median follow-u overall survival was 9·99 months (IQR 6·05–15·05). Median overall survival was 10·3 months (95% CI 8·7–11 the group that received in the nab-paclitaxel every 3 weeks, 11·1 months (9·9–13·0) in the weekly nab-paclitaxel g and 10·9 months (9·4–11·8) in the weekly solvent-based paclitaxel group. Weekly nab-paclitaxel was non-infe weekly solvent-based paclitaxel (hazard ratio 0·97, 97·5% CI 0·76–1·23; non-inferiority one-sided p=0·0085, wh nab-paclitaxel every 3 weeks was not non-inferior to solvent-based paclitaxel (1·06, 95% CI 0·87–1·31; non-infe one-sided p=0·062). The main grade 3 or worse adverse drug reactions were neutropenia (158 [65%] of 244 patie



	白紫（3周 260mg/M2）	白紫（周疗 100mg/M2）	力扑素（周疗 80mg/M2）
PFS	3.8m	**5.3m**	3.8m
OS	10.3m	11.1m	10.9m

非劣效性研究

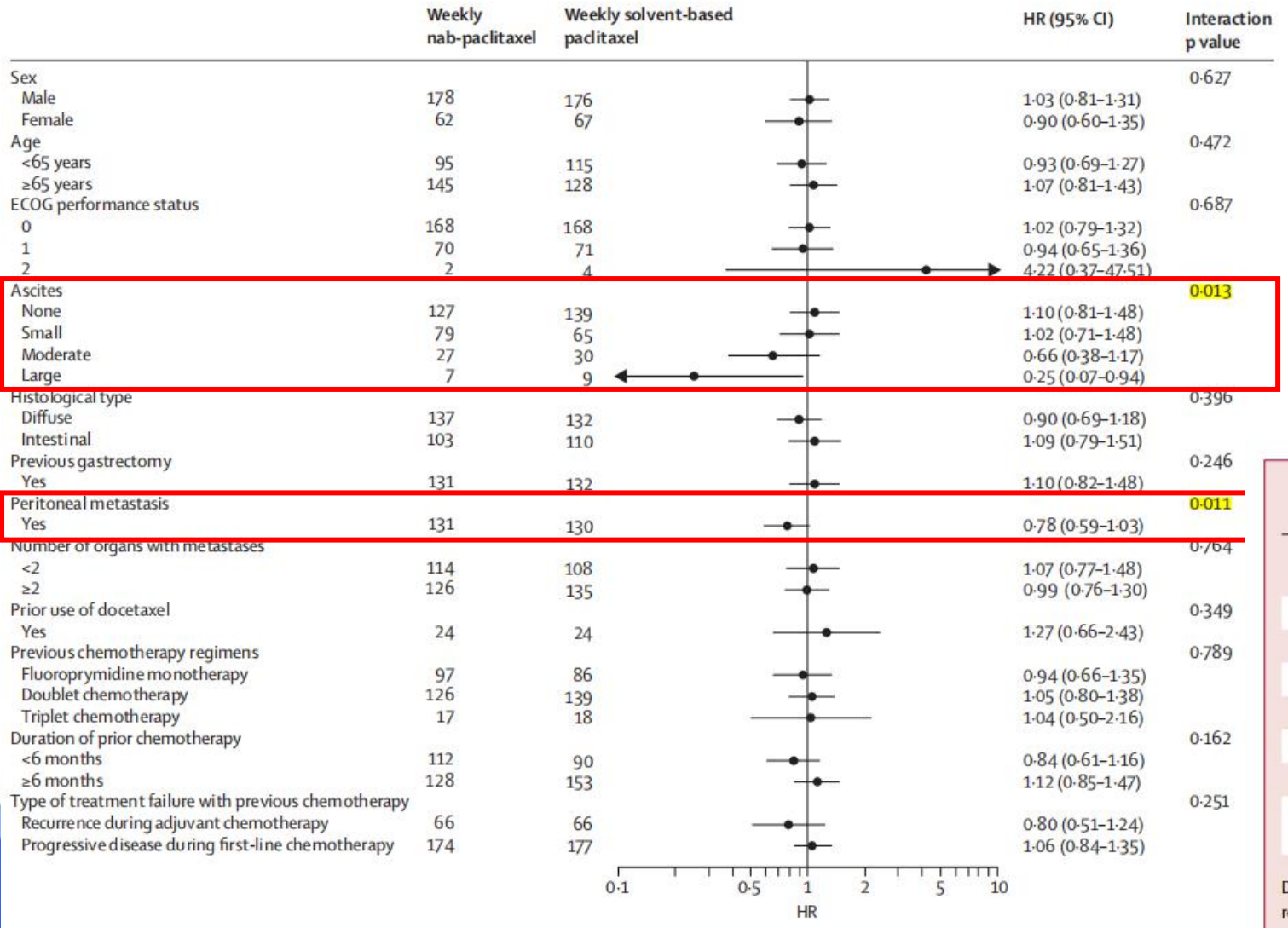


Figure 3: **Forest plots for subgroup analyses of overall survival**

	Nab-paclitaxel every three weeks (n=243)	Weekly nab-paclitaxel (n=240)	Weekly solvent-based paclitaxel (n=243)
Total number of assessable participants	150	150	169
Complete response	2 (1%)	4 (3%)	3 (2%)
Partial response	36 (24%)	45 (30%)	38 (22%)
Stable disease	62 (41%)	63 (42%)	78 (46%)
Progressive disease	49 (33%)	37 (25%)	50 (30%)
Not evaluable	1 (1%)	1 (1%)	0
Overall response*	38 (25%)	49 (33%)	41 (24%)
Overall response 95% CI, p value	18·6–33·1, p=0·897†	25·2–40·8, p=0·106†	18·0–31·4

Data are n (%), unless otherwise specified. *Overall response was calculated as number of patients who had a complete response plus number of patients who had a partial response. †Versus weekly solvent-based paclitaxel (Fisher's exact test).

Table 2: **Tumour responses according to Response Evaluation Criteria in Solid Tumors version 1.1**

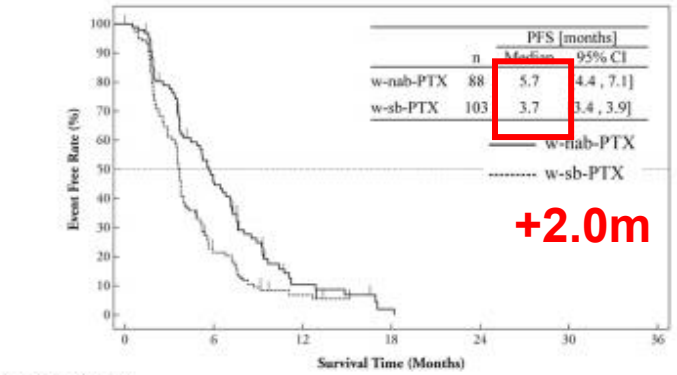
ORIGINAL ARTICLE

Peritoneal metastasis as a predictive factor for nab-paclitaxel in patients with pretreated advanced gastric cancer: an explo analysis of the phase III ABSOLUTE trial

Results This study included 240 and 243 patients in the w-nab-PTX and w-sb-PTX arms, r the w-nab-PTX arm ($n=88$) had longer OS than the w-sb-PTX arm ($n=103$), and median s 8.7 months [hazard ratio (HR) 0.63; 95% CI 0.45–0.88; $P=0.0060$], respectively. In the no P ($n=140$) had shorter OS than the w-sb-PTX arm ($n=152$), and MST of 11.6 and 15.7 months $P=0.0180$), respectively. After adjusting for prognostic factors, the HR for OS in the w-nab-l arm was 0.59 (95% CI 0.42–0.83; $P=0.0023$; PM group) and 1.34 (95% CI 1.01–1.78; $P=$ significant interaction between treatment efficacy and presence of peritoneal metastasis ($P=$

a Progression-free survival

PM group

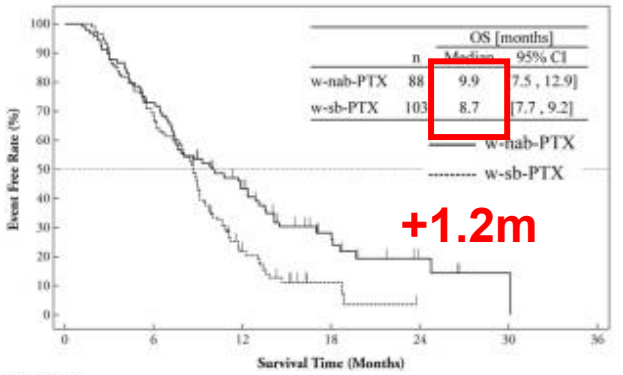


Number at risk (%)

w-nab-PTX	88 (100.0)	37 (45.9)	6 (10.9)	1 (2.4)		
w-sb-PTX	103 (100.0)	20 (21.7)	5 (7.2)	0		

b Overall survival

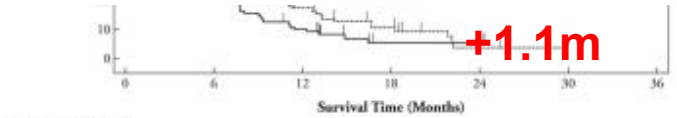
PM group



Number at risk (%)

w-nab-PTX	88 (100.0)	64 (72.7)	33 (43.4)	13 (28.3)	4 (19.4)	1 (14.5)
w-sb-PTX	103 (100.0)	71 (68.9)	19 (21.9)	3 (11.5)	0	0

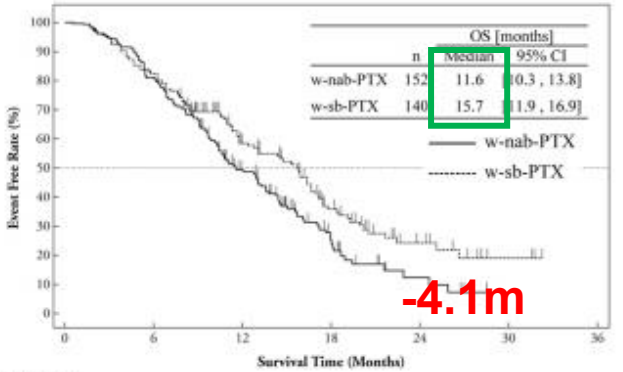
No PM group



Number at risk (%)

w-nab-PTX	152 (100.0)	42 (28.8)	13 (10.4)	2 (5.8)	2 (5.8)	0
w-sb-PTX	140 (100.0)	36 (28.2)	20 (17.7)	10 (10.9)	2 (3.9)	0

No PM group



Number at risk (%)

w-nab-PTX	152 (100.0)	123 (80.9)	63 (49.3)	20 (25.3)	5 (12.3)	0
w-sb-PTX	140 (100.0)	115 (82.1)	68 (58.4)	34 (36.0)	12 (24.4)	3 (19.2)

Gastric Cancer. 2021 Mar;24(2):467-476. doi: 10.1007/s10120-020-01131-y. Epub 2020 Nov 2.

Effect of early tumor response on the health-related quality of life among patients on second-line chemotherapy for advanced gastric cancer in the ABSOLUTE trial

胃癌 FOXAGAST研究（围手术期）

ELSEVIER

journal homepage: www.ejcancer.com

Original Research

Oxaliplatin, 5-Fluorouracil and Nab-paclitaxel as perioperative regimen in patients with resectable gastric adenocarcinoma: A GERCOR phase II study (FOXAGAST)

Results: Forty-nine patients were included. Median number of neoadjuvant chemotherapy cycles was 6 (range, 3–6). Median dose intensity for Nab-paclitaxel, oxaliplatin and 5-FU was 96% (38–103%), 97% (47–103%) and 99% (50–112%), respectively. Surgery could not be performed in 5 (10.2%) patients. Tumour resection was R0 for 42 of 44 (95.5%) patients. Pathological review classified tumours as TRG1 to TRG5 for 8 (16.3%), 11 (22.5%), 4 (8.2%), 18 (36.7%) and 3 (6.1%) patients, respectively. Grade 3 or worse toxicities during neoadjuvant

to Mandard TRG classification, with TRG1 corresponding to cPR, TRG2 major pathological response with few residual tumour cells, TRG3 fibrosis and tumour cells with a dominance of fibrosis, TRG4 fibrosis and tumour cells with a dominance of tumour cells, and TRG5 tumour without evidence of regression. The histological tumour type was determined according to Lauren's classification [22].

Table 2
Pathological tumour stage, nodal status and outcome.

Patient characteristics	All patients
Pathological T stage (N = 44)	
- ypT0	8 (18.2)
- ypT1	6 (13.6)
- ypT2	7 (15.9)
- ypT3	19 (43.2)
- ypT4	3 (6.8)
- Unknown	1 (2.3)
Pathological N stage (N = 44)	
- ypN0 (0)	29 (65.9)
- ypN1 (1–6)	11 (25.0)
- ypN2 (7–15)	3 (6.8)
- ypN3 (>15)	1 (2.3)
Pathological response (N = 49)	
- TRG1	8 (16.3)
- TRG2	11 (22.5)
- TRG3	4 (8.2)
- TRG4	18 (36.7)
- TRG5	3 (6.1)
- Not applicable[a]	5 (10.2)

- 肿瘤缩退分级
  - ✓ TRG1：完全病理反应（cPR）
  - ✓ TRG2：近完全病理反应，少量肿瘤细胞
  - ✓ TRG3：纤维化，肿瘤细胞具有纤维支配
  - ✓ TRG4：纤维化，肿瘤细胞占据优势
  - ✓ TRG5：肿瘤无退行现象

目录

3.4.1 转移性胰腺癌一线治疗

分层	Ⅰ级专家推荐	Ⅱ级专家推荐	Ⅲ级专家推荐
体能状态良好	1. GEM（1A 类证据） 2. 替吉奥单药（1A 类证据） 3. GEM+ 白蛋白结合型紫杉醇（1A 类证据） 4. FOLFIRINOX 方案（1A 类证据） 5. 含铂类的方案（存在 *BRCA1/2* 胚系突变），对于治疗≥ 16 周后仍无疾病进展的患者，考虑奥拉帕利维持治疗（1A 类证据）	1. GEM 联合替吉奥方案（1B 类证据） 2. GEM 联合尼妥珠单抗（2A 类证据） 3. 参加临床研究	1. GEM 联合厄洛替尼方案（1A 类证据） 2. GEM 联合 CAP 方案（1B 类证据） 3. 其他方案：GEM+顺铂；固定剂量率 GEM、多西他赛、卡培他滨；氟尿嘧啶类 + 奥沙利铂
体能状态较差	1. GEM（1A 类证据） 2. 替吉奥单药（1A 类证据） 3. 最佳支持治疗 4. 参加临床研究		

GEM+ 白蛋白结合型紫杉醇方案 [a]
白蛋白结合型紫杉醇 125mg/m^2 静脉输注，d1、8、15
GEM 1 000mg/m^2 静脉输注大于 30min，d1、8、15
每 4 周重复 1 次

可调整 GEM+ 白蛋白结合型紫杉醇方案
白蛋白结合型紫杉醇 125mg/m^2 静脉输注，d1、8
GEM 1 000mg/m^2 静脉输注大于 30min，d1、8
每 3 周重复 1 次

The NEW ENGLAND JOURNAL of MEDICINE

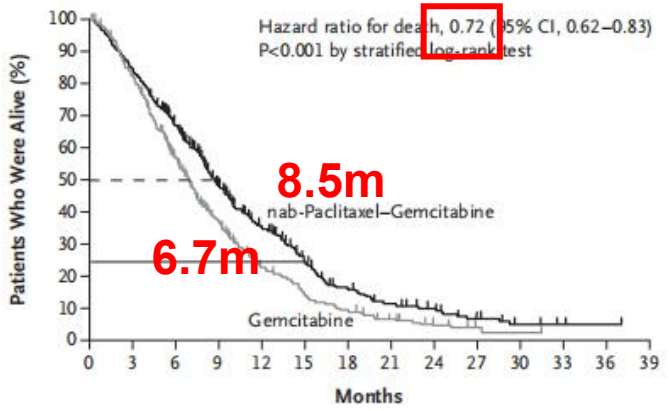
ORIGINAL ARTICLE

Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine

RESULTS

A total of 861 patients were randomly assigned to nab-paclitaxel plus gemcitabine (431 patients) or gemcitabine (430). The median overall survival was 8.5 months in the nab-paclitaxel–gemcitabine group as compared with 6.7 months in the gemcitabine group (hazard ratio for death, 0.72; 95% confidence interval [CI], 0.62 to 0.83; P<0.001). The survival rate was 35% in the nab-paclitaxel–gemcitabine group versus 22% in the gemcitabine group at 1 year, and 9% versus 4% at 2 years. The median progression-free survival was 5.5 months in the nab-paclitaxel–gemcitabine group, as compared with 3.7 months in the gemcitabine group (hazard ratio for disease progression or death, 0.69; 95% CI, 0.58 to 0.82; P<0.001); the response rate according to independent review was 23% versus 7% in the two groups (P<0.001). The most common adverse events of grade 3 or higher were neutropenia (38% in the nab-paclitaxel–gemcitabine group vs. 27% in the gemcitabine group), fatigue (17% vs. 7%), and neuropathy (17% vs. 1%). Febrile neutropenia occurred in 3% versus 1% of the patients in the two groups. In the nab-paclitaxel–gemcitabine group, neuropathy of grade 3 or higher improved to grade 1 or lower in a median of 29 days.

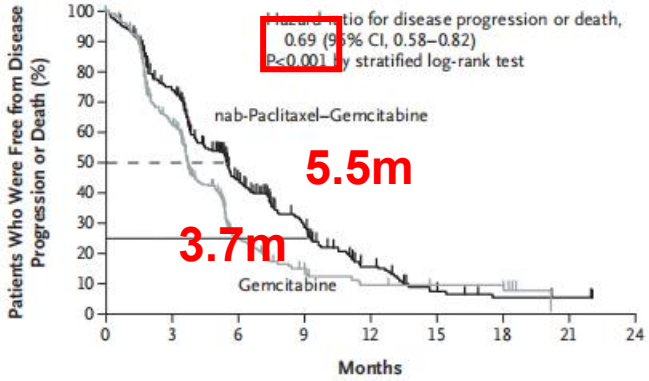
A Overall Survival



No. at Risk

nab-Paclitaxel–Gemcitabine	431	357	269	169	108	67	40	27	16	9	4	1	1	0
Gemcitabine	430	340	220	124	69	40	26	15	7	3	1	0	0	0

B Progression-free Survival, According to Independent Review



No. at Risk

nab-Paclitaxel–Gemcitabine	431	281	122	62	24	8	4	2	0
Gemcitabine	430	209	51	23	10	6	4	0	0

ORR: 23%　7%

胰腺导管腺癌一线化疗方案：FOLFIRINOX方案 vs. 吉西他滨联合白蛋白结合型紫杉醇，哪个更好?

JAMA Surg.2020 Sep 1;155(9):832-839. doi: 10.1001/jamasurg.2020.2286.

JAMA Surgery | Original Investigation

Response and Survival Associated With First-line FOLFIRINOX vs Gemcitabine and nab-Paclitaxel Chemotherapy for Localized Pancreatic Ductal Adenocarcinoma

Characteristic	Univariable HR (95% CI)	*P* value	Multivariable HR (95% CI)	*P* value
Female sex	1.19 (0.67-2.13)	.50	NA	NA
BMI	1.01 (0.96-1.07)	.70	NA	NA
First-line chemotherapy regimen				
FOLFIRINOX	1 [Reference]			
GA	1.50 (1.00-2.26)	.05	1.48 (0.97-2.26)	.07
Baseline CA 19-9 level, U/mL	1.01 (0.99-1.03)	.30	NA	NA
Tumor site				
Head or neck	1 [Reference]			
Body or tail	0.78 (0.39-1.56)	.50	NA	NA
No. of chemotherapy cycles	0.72 (0.52-1.01)	.06	0.73 (0.52-1.02)	.06

Table 4. Univariate and Multivariate Cox Proportional Hazards Regression Analysis of Overall Survival for All 485 Patients

Characteristic	No. (%) of patients: All (n = 280)	First-line chemotherapy regimen: FOLFIRINOX (n = 140)	GA (n = 140)	*P* value
Radiographic measures after treatment				
Reduction in primary tumor volume				
Yes	197 (70)	100 (71)	97 (69)	.70
No	83 (30)	40 (29)	43 (31)	
%Δvol, Median (range)	20 (−240 to 90)	30 (−240 to 90)	10 (−150 to 90)	.10
RECIST 1.1				.001
CR	0	0	0	
PR	35 (13)	27 (19)	8 (6)	
SD	219 (78)	102 (73)	117 (83)	
PD	26 (9)	11 (8)	15 (11)	
Local tumor downstaging[a]				.70
Yes[b]	13 (8)	7 (8)	6 (7)	
No[b]	154 (92)	79 (92)	75 (93)	
Serologic measures after treatment				
Posttreatment CA 19-9 level, median (range), U/mL	59 (1 to 11 570)	59 (1 to 5813)	63 (1 to 11 570)	.70
Change in CA 19-9				.90
Not expressed	14 (5)	7 (5)	7 (5)	
Normal to normal	41 (15)	22 (16)	19 (14)	
Elevated to normal	59 (21)	31 (22)	28 (20)	
Elevated to elevated	161 (58)	78 (56)	83 (59)	
Normal to elevated	5 (2)	2 (1)	3 (2)	

FOLFIRINOX　ORR率高，但两者OS无差异

6.1 胆道恶性肿瘤的新辅助治疗

内容	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
新辅助化疗	参加临床试验[a]	吉西他滨 + 顺铂 + 白蛋白紫杉醇（2A 类）[b][1] 5-FU+ 奥沙利铂（2A 类） 卡培他滨 + 奥沙利铂（2A 类） 吉西他滨 + 卡培他滨（2A 类） 吉西他滨 + 顺铂（2A 类） 5-FU+ 顺铂（2B 类） 卡培他滨 + 顺铂（2B 类） 吉西他滨 + 奥沙利铂（2B 类）	

National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2021
Biliary Tract Cancers

PRINCIPLES OF SYSTEMIC THERAPY

Neoadjuvant Therapy[a]

Preferred Regimens
- None

Other Recommended Regimens
- 5-fluorouracil + oxaliplatin
- Capecitabine + oxaliplatin
- Gemcitabine + capecitabine
- Gemcitabine + cisplatin
- Gemcitabine + cisplatin + albumin-bound paclitaxel[1] (category 2B)
- Gemcitabine + oxaliplatin (category 2B)
- Single agents:
  - 5-fluorouracil
  - Capecitabine
  - Gemcitabine

吉西他滨 + 顺铂 + 白蛋白紫杉醇

吉西他滨 1 000mg/m² 静脉滴注 30min，d1、8
顺铂 25mg/m² 静脉滴注，d1、8
白蛋白紫杉醇 125mg/m² 静脉滴注，d1、8
每 3 周重复

6.3 晚期胆道恶性肿瘤的一线治疗

分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
可耐受强烈化疗的患者[a]	吉西他滨联合顺铂（1A 类）[1] 吉西他滨联合替吉奥（1A 类）[2] 卡培他滨 + 奥沙利铂（1A 类）[3]	吉西他滨 + 顺铂 + 白蛋白紫杉醇（2B 类）[b][4] 吉西他滨 + 顺铂 + 替吉奥（2B 类）[5] 吉西他滨 + 奥沙利铂（2A 类）[6] 5-FU+ 奥沙利铂（2A 类） 5-FU+ 顺铂（2A 类） 卡培他滨 + 顺铂（2A 类） 吉西他滨 + 卡培他滨（2A 类） 吉西他滨或 5-FU 为基础的方案（2A 类） 吉西他滨 + 白蛋白紫杉醇（仅限于胆管癌）（2A 类） *NTRK* 基因融合阳性肿瘤[c] 恩曲替尼[8] 拉罗替尼[9] MSI-H/dMMR 肿瘤[c] 帕博利珠单抗[10] 卡瑞利珠单抗联合 GEMOX（2B 类）[d][11, 12]	纳武利尤单抗 + 吉西他滨 + 顺铂（2A 类）[d] GEMOX+ 仑伐替尼 + 特瑞普利单抗（2B 类）[13] 参加临床试验[e]
不能耐受强烈化疗的患者	吉西他滨单药（1B 类）	替吉奥 /5-FU/ 卡培他滨单药（2A 类）	

National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2021
Biliary Tract Cancers

PRINCIPLES OF SYSTEMIC THERAPY

Primary Treatment for Unresectable and Metastatic Disease

Preferred Regimens
- Gemcitabine + cisplatin[4] (category 1)

Other Recommended Regimens
- 5-fluorouracil + oxaliplatin
- 5-fluorouracil + cisplatin (category 2B)
- Capecitabine + cisplatin (category 2B)
- Capecitabine + oxaliplatin
- Gemcitabine + albumin-bound paclitaxel
- Gemcitabine + capecitabine
- Gemcitabine + oxaliplatin
- Gemcitabine + cisplatin + albumin-bound paclitaxel[1] (category 2B)
- Single agents:
  - 5-fluorouracil
  - Capecitabine
  - Gemcitabine

JAMA Oncology | Original Investigation

Gemcitabine, Cisplatin, and nab-Paclitaxel for the Treatment of Advanced Biliary Tract Cancers

A Phase 2 Clinical Trial

62例

INTERVENTIONS Patients initially received gemcitabine, 1000 mg/m^2, cisplatin, 25 mg/m^2, and nab-paclitaxel, 125 mg/m^2, on days 1 and 8 of 21-day cycles. Owing to hematologic adverse events among the first 32 patients enrolled, these starting doses were reduced to 800, 25, and 100 mg/m^2, respectively, for the remaining 28 patients.

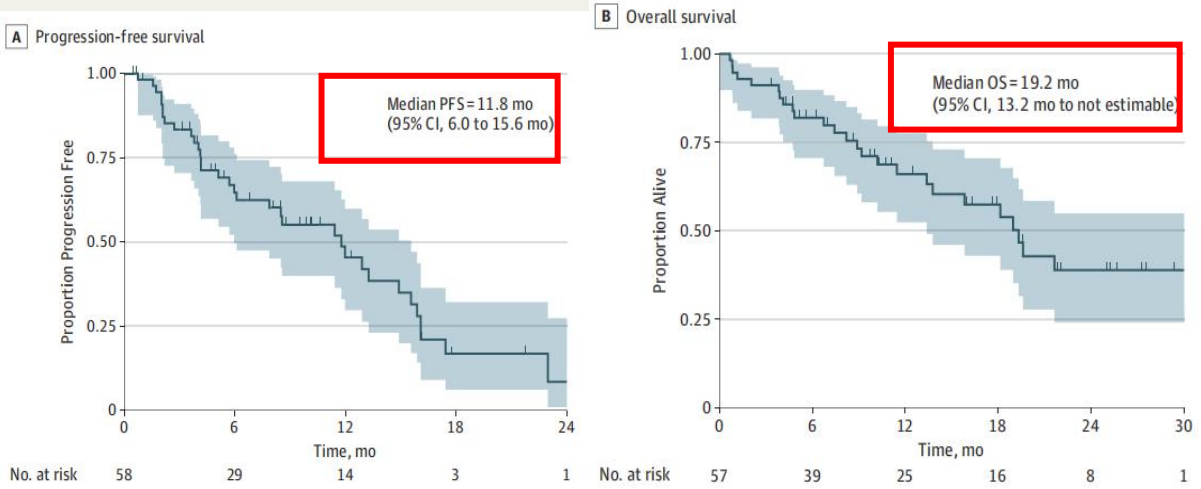
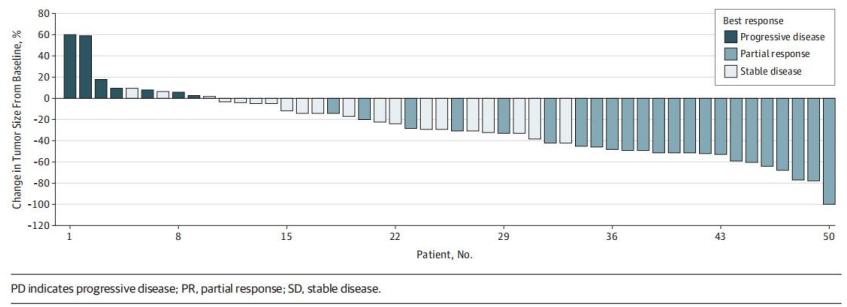


Figure 3. Change in Tumor Size From Baseline to Best Response Among 50 Patients in the Intention-to-Treat Population for Whom Data Were Available



PD indicates progressive disease; PR, partial response; SD, stable disease.

ORR为**45%**

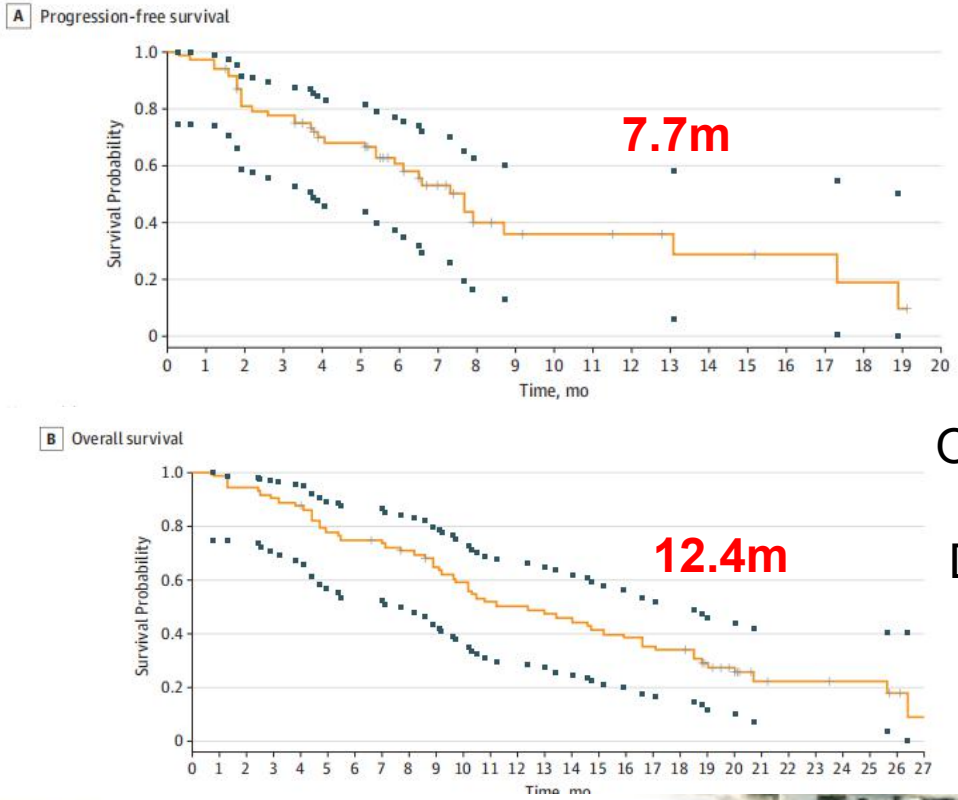
DCR为**84%**

JAMA Oncology | Original Investigation

Nab-Paclitaxel and Gemcitabine as First-line Treatment of Advanced or Metastatic Cholangiocarcinoma

A Phase 2 Clinical Trial

INTERVENTIONS Patients received intravenous nab-paclitaxel, 125 mg/m^2, followed by gemcitabine, 1000 mg/m^2, on days 1, 8, and 15 of each 28-day treatment cycle until disease progression or unacceptable toxic effects.



ORR为**30%**

DCR为**60%**

目录

分期	分层 1	分层 2	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
T1-2N+/T3-4 任何 N	适宜手术患者		手术 ± 放疗 / 放化疗[1]（2A 类）		
	不适宜手术患者	适宜使用顺铂患者	放疗 + 顺铂[15-17]（1A 类）	诱导化疗→单纯放疗[18-20]（1B 类）	

常用的诱导化疗方案是 TPF（多西他赛 75mg/m^2，第 1 天；顺铂 75mg/m^2，第 1 天；5-FU 750mg/m^2，第 1~5 天；每 3 周重复，连续 3 个周期）[18-20]。针对这部分患者，与直接同期放化疗相比，诱

5.1 复发 / 转移性头颈部鳞癌（非鼻咽癌）的治疗

分期	分层 1	分层 2	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
局部和 / 或颈部复发	适宜手术患者		手术[1-2]（2A 类）		
	不适宜手术患者	既往未行放疗	放疗[1-2]（2A 类）		
		既往行放疗	参照远处转移	再程放疗[1-2]（2A 类）	
远处转移		一线治疗	帕博利珠单抗 + 顺铂 / 卡铂 + 5-FU[3]（1A 类） 帕博利珠单抗（CPS ≥ 1）[3]（1A 类） 顺铂 / 卡铂 +5-FU+ 西妥昔单抗[4-6]（1A 类） 顺铂 + 多西他赛 + 西妥昔单抗[7]（1A 类） 顺铂 / 卡铂 + 紫杉醇 ± 西妥昔单抗[8, 9]（2A 类）	顺铂 / 卡铂 +5-FU[10]（1A 类） 顺铂 + 西妥昔单抗[11, 12]（2A 类） 紫杉醇 + 西妥昔单抗[13]（2A 类）	
		二线或挽救治疗	纳武利尤单抗[14-16]（1A 类）	帕博利珠单抗[17]（1A 类） 甲氨蝶呤[18]（2A 类） 多西他赛[19]（2A 类） 紫杉醇[20]（2A 类） 西妥昔单抗[21]（2A 类）	阿法替尼[22, 23]（1A 类）

5.2 复发 / 转移性鼻咽癌的治疗

分期	分层 1	分层 2	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
局部或颈部复发	适宜手术患者	局部复发	手术（2A 类）[1] 再程放疗（2A 类）[2, 3]	参照远处转移	
		颈部复发	手术（2A 类）[2, 3]		
	不适宜手术患者		再程放疗（2A 类）[2, 3]	参照远处转移	
远处转移		一线治疗	顺铂 + 吉西他滨[4]（1A 类） 顺铂 + 多西他赛[5, 6]（2A 类） 卡铂 + 紫杉醇[7]（2A 类）	顺铂 / 卡铂 +5-FU[8, 9]（2A 类） 顺铂 + 卡培他滨[10, 11]（2A 类）	卡瑞利珠单抗 + 顺铂 + 吉西他滨[12]（2B 类）
		二线或挽救治疗		吉西他滨[13]（2A 类） 多西他赛[14]（2A 类） 卡培他滨[15]（2A 类） 特瑞普利单抗[16]（2A 类）	卡瑞利珠单抗[12]（2B 类） 帕博利珠单抗[17]（2B 类） 纳武利尤单抗[18]（2B 类）

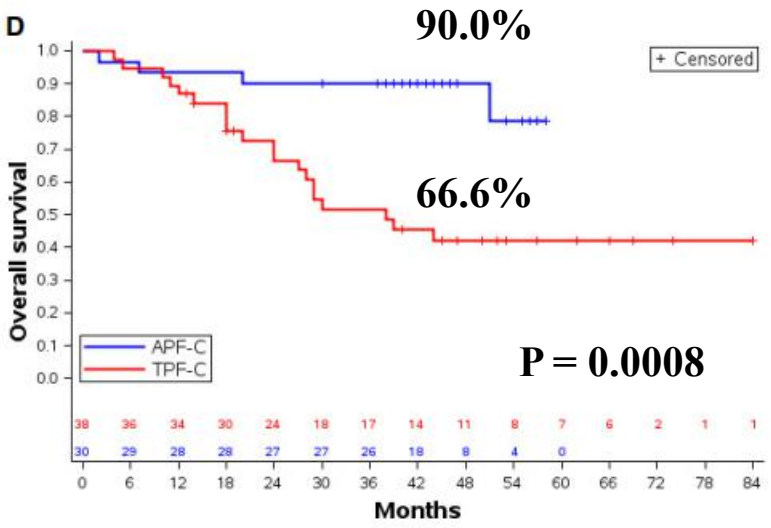
Cancer Medicine

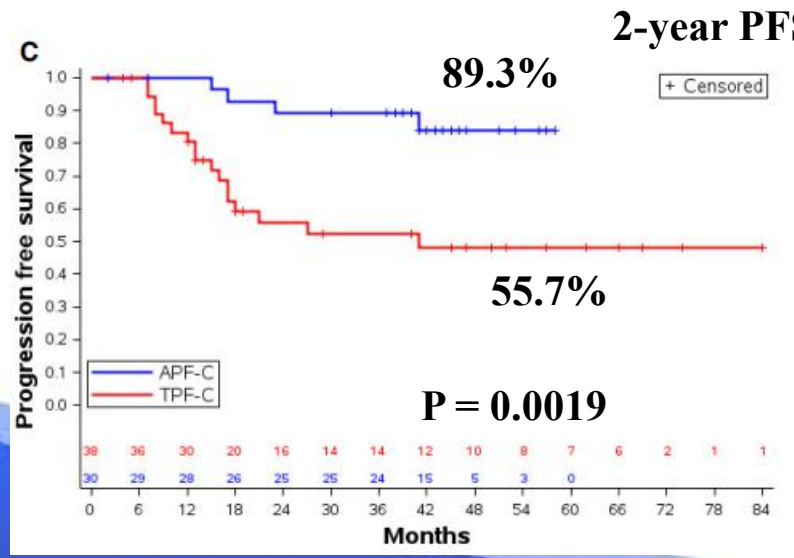
Open Access

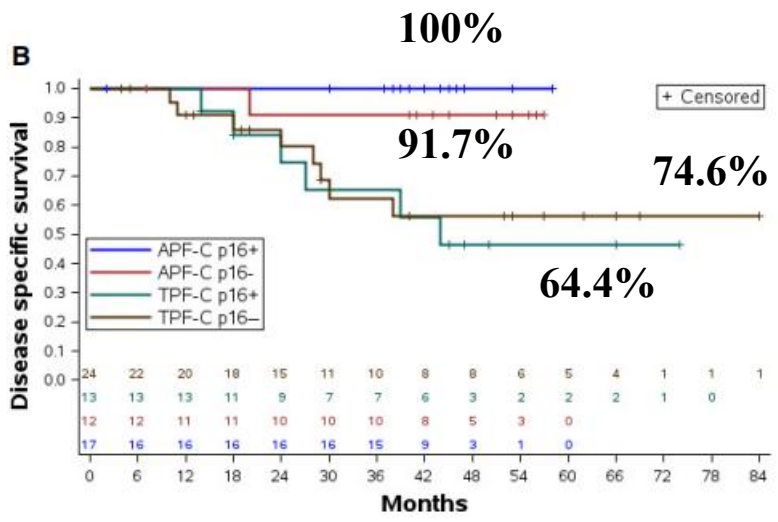
ORIGINAL RESEARCH

Nab-paclitaxel-based compared to docetaxel-based induction chemotherapy regimens for locally advanced squamous cell carcinoma of the head and neck

compare the disease-specific survival (DSS) and overall survival (OS) between patients given *nab*-paclitaxel, cisplatin, and fluorouracil with cetuximab (APF-C) and historical controls given docetaxel, cisplatin, and fluorouracil with cetuximab (TPF-C). Patients with locally advanced HNSCC were treated with APF-C ($n = 30$) or TPF-C ($n = 38$). After 3 cycles of IC, patients were scheduled to receive cisplatin concurrent with definitive radiotherapy. T and N clas-







3.3 皮肤黑色素瘤的晚期治疗原则

3.3.1 无脑转移患者的治疗

分期	分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
转移性或不可切除Ⅲ或Ⅳ期患者的治疗	一线	如携带 *BRAF V600* 突变：达拉非尼 + 曲美替尼（1 类） 达卡巴嗪 / 替莫唑胺 ± 铂类 ± 恩度	帕博利珠单抗 特瑞普利单抗 如携带 *BRAF V600* 突变：维莫非尼 如携带 *KIT* 突变：伊马替尼 如肿瘤负荷偏大或减瘤为首要目的：紫杉醇 / 白蛋白紫杉醇 ± 铂类 ± 抗血管药物	纳武利尤单抗 PD-1 单抗 + 伊匹木单抗 一般状况较差的患者可考虑采用最佳支持治疗 如携带 *BRAF V600* 突变：维莫非尼 / 考比替尼 + 阿替利珠单抗或达拉非尼 / 曲美替尼 + 帕博利珠单抗

4.3 肢端黑色素瘤的晚期治疗原则

4.3.1 无脑转移患者的治疗

分期	分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
转移性或不可切除Ⅲ或Ⅳ期患者的治疗	一线	如携带 *BRAF V600* 突变：达拉非尼 + 曲美替尼（1 类） 达卡巴嗪 / 替莫唑胺 ± 铂类 ± 恩度	如携带 *BRAF V600* 突变：维莫非尼 如携带 *KIT* 突变：伊马替尼 如肿瘤负荷偏大或减瘤为首要目的：紫杉醇 / 白蛋白紫杉醇 ± 铂类 ± 抗血管药物	帕博利珠单抗 特瑞普利单抗 纳武利尤单抗 阿帕替尼 + 卡瑞利珠单抗 PD-1 单抗 + 伊匹木单抗 一般状况较差的患者可考虑采用最佳支持治疗 如携带 *BRAF V600* 突变：

白蛋白结合型紫杉醇 ± 卡铂 ± 贝伐珠单抗：白蛋白结合型紫杉醇 260mg/m^2 d1 ± 卡铂 AUC=5，± 贝伐珠单抗 5mg/kg d1/15，每 4 周一次。

不可手术切除或晚期黏膜黑色素瘤

分期 [a]	分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
不可切除或者Ⅳ期	不可手术切除局部晚期	化疗 + 抗血管生成药物 [k]	特瑞普利单抗 + 阿昔替尼 [n] 伊马替尼 [o]（CKIT 突变）± 局部放疗 [g]（头颈部）	帕博利珠单抗 [p] 特瑞普利单抗 [p] 阿替利珠单抗 + 贝伐珠单抗 [m]
	任何 T，任何 N，M1	维莫非尼 [l]（BRAF V600 突变） 达拉非尼 + 曲美替尼 [m]（BRAF V600 突变）		

眼部葡萄膜黑色素瘤的治疗原则

分期 [a]	分层	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
Ⅰ、Ⅱ、Ⅲ期	手术方式	眼球摘除术 [b] 或巩膜表面敷贴器放射治疗 [c]	肿瘤局部切除术 [d] 或眶内容剜除术 [e]	
	术后辅助治疗	临床研究	大剂量干扰素 [f]	
Ⅳ期	任何 T，任何 N，M1	临床研究	化疗 + 抗血管生成药物 [g] 如有肝转移，同时联合肝动脉化疗栓塞 [h]	如有肝转移，行肝转移灶瘤体注射 [i] ipilimumab [j] MEK 抑制剂 [k] PD-1 单抗 [l]

低瘤负荷转移性激素敏感性前列腺癌的治疗选择

Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
ADT 为基础的联合治疗[a]	ADT+ 多西他赛 ± 泼尼松[g]（1B 类）	间歇性 ADT（2B 类）
ADT+ 醋酸阿比特龙 + 泼尼松[b]（1A 类）	原发灶手术切除或者近距离放疗[h]（2A 类）	ADT+ 冷冻治疗[i]（3 类）
ADT+EBRT[c]（1A 类）		ADT+ 氟他胺[f]（2A 类）
ADT+ 恩扎卢胺[d]（1A 类）		
ADT+ 阿帕他胺[e]（1A 类）		
ADT+ 比卡鲁胺[f]（2A 类）		

高瘤负荷转移性激素敏感性前列腺癌的治疗选择

Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
ADT+ 醋酸阿比特龙 + 泼尼松[b]（1A 类）	ADT+ 比卡鲁胺[f]（2A 类）	ADT+ 氟他胺[f]（2A 类）
ADT+ 多西他赛 ± 泼尼松[g]（1A 类）	原发灶手术切除或者近距离放疗[h]（2A 类）	
ADT+ 恩扎卢胺[d]（1A 类）		
ADT+ 阿帕他胺[e]（1A 类）		

8.2.2 转移性去势抵抗性前列腺癌的治疗

分级治疗阶段	Ⅰ级推荐	Ⅱ级推荐	Ⅲ级推荐
既往未经新型内分泌治疗和化疗	阿比特龙 / 泼尼松[a]（1A 类） 恩扎卢胺[b]（1A 类） 多西他赛[c]（1A 类） 镭 -223[d]（有症状的骨转移患者）	Sipuleucel-T[e]（1B 类）	其他二线内分泌治疗（3 类）
既往新型内分泌治疗失败且未经化疗	多西他赛（1A 类） 奥拉帕利[f]（1A 类） 镭 -223（有症状的骨转移患者）（1A 类）	恩扎卢胺 / 阿比特龙 / 泼尼松（2A 类） Sipuleucel-T 卡巴他赛[g]（1A 类）	阿比特龙 / 地塞米松（3 类）[h]
既往多西他赛化疗失败且未经新型内分泌治疗	阿比特龙 / 泼尼松（1A 类） 恩扎卢胺（1A 类） 奥拉帕利（1B 类） 镭 -223（有症状的骨转移患者）（1A 类）	卡巴他赛（1A 类）	

Phase II Trial of Neoadjuvant Nab-Paclitaxel in High Risk Patients With Prostate Cancer Undergoing Radical Prostatectomy

D. R. Shepard,* R. Dreicer,† J. Garcia, P. Elson, C. Magi-Galluzzi, D. Raghavan, A. J. Stephenson and E. A. Klein

小结

1.乳腺癌　新辅助 GBG69研究白紫较紫杉醇脂质体提高了接近10%PCR率；对于晚期患者白紫应用较紫杉醇脂质体、多西他赛 ORR率提高14%-20%。

2.肺鳞癌　亚组分析显示晚期白紫+免疫相较于紫杉醇+免疫能降低5-10%死亡或进展风险；白紫维持治疗可延长OS.

3.食管癌　白紫联合铂类相较于紫杉醇ORR率提高20%。

4.胃癌　ABSOLUTE研究提示大量腹水、腹膜转移患者应用白紫疗效佳。

5.胰腺癌　围手术期FOLFIRINOX 较白紫+吉西他滨ORR率更高，但两者OS无明显差异。

6.胆管癌　白紫+顺铂+吉西他滨 PFS 11.8m ，ORR 45%

7.头颈部鳞癌　TPF，白紫较多西他赛 2年PFS率提高35%，2年OS率提高25%。

8. 黑色素瘤　白紫在各种类型黑色瘤均可应用。

9.前列腺癌　白紫替换多西他赛证据尚不充分，临床研究不多。

Thanks !