Case #4
Management of Recurrent Triple-Negative Breast Cancer: What's the Best Approach?

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Clinical Case Summary

- 44-year-old female
- Triple-negative breast cancer
- Recurrence of disease in lung and liver 12 months after completion of adjuvant anthracycline and taxane chemotherapy
- Symptomatic
- ECOG PS: 1
- No comorbid illnesses

Part I

Is this patient anthracycline/taxane resistant?

1. Yes
2. No

Part II

Which of the following systemic therapy options would you choose for this patient at the time of progression?

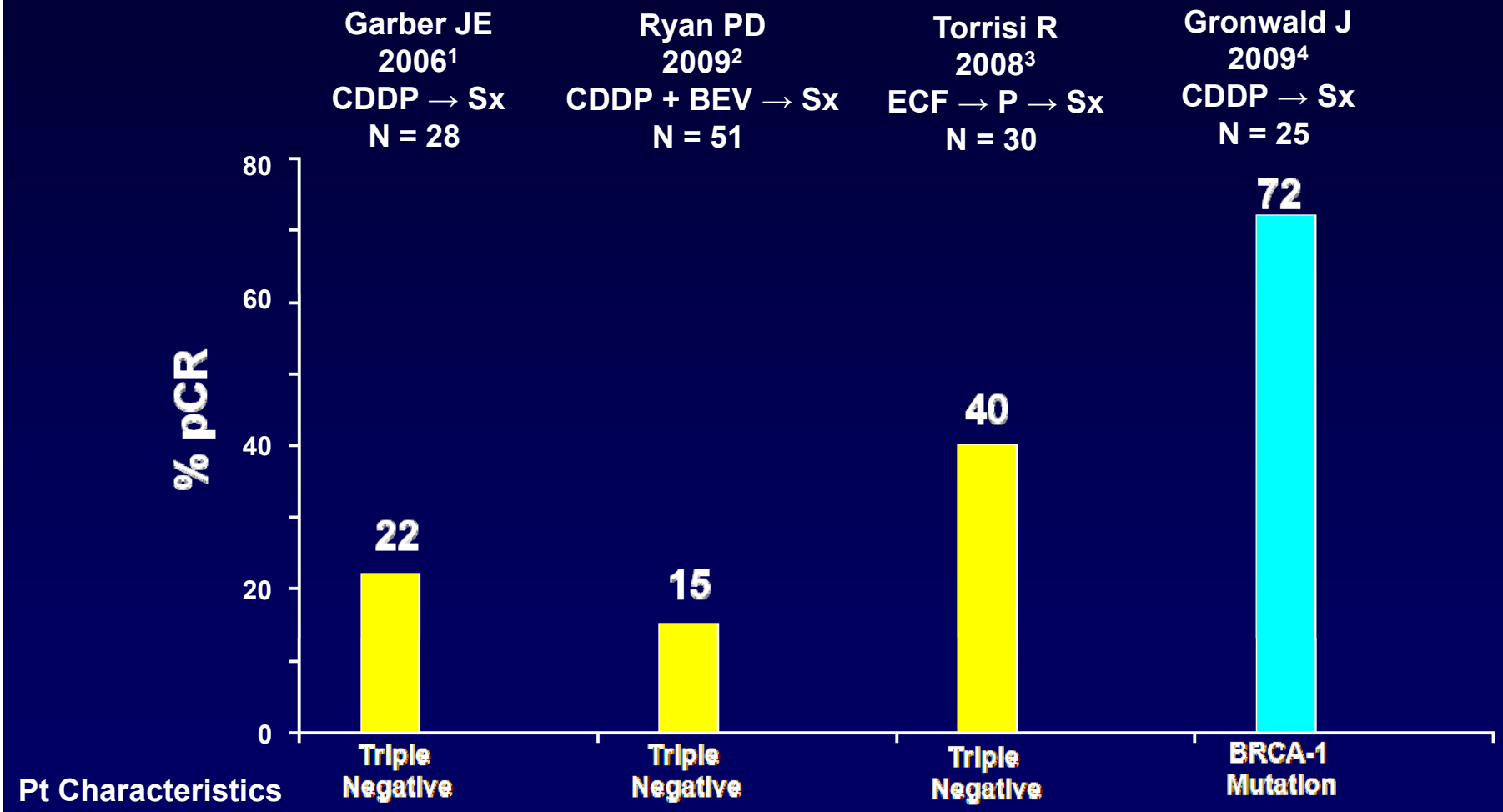
1. Combination chemotherapy (eg, capecitabine + docetaxel, gemcitabine + paclitaxel)
2. Single-agent chemotherapy
3. Platinum-based chemotherapy
4. Chemotherapy + bevacizumab
5. Clinical trial with PARP inhibitor and chemotherapy

Chemotherapy for Metastatic Breast Cancer (MBC)

- **Sequential single agents preferred for most patients**
  - Variety of options—no single 'gold standard'
  - Limits toxicity
  - Supported by clinical trial data
- **Combinations appropriate for rapidly progressive symptomatic disease**
  - Reduction in symptoms outweighs potential toxicity
  - May not be candidate for subsequent therapy if continued progression

Why Platinum Based Chemotherapy?

Neoadjuvant Chemotherapy with Platinum-Compounds: Phase II Trials



CDDP, cisplatin; Sx, surgery; BEV, bevacizumab; ECF, epirubicin-cisplatin-5FU; P, paclitaxel; pCR, pathologic complete response

1. Garber JE, et al. *Breast Cancer Res Treat.* 2006;100(Suppl 1): Abstract 3074. 2. Ryan PD, et al. *J Clin Oncol.* 2009;27(15S): Abstract 551. 3. Torrisi R, et al. *Cancer Chemother Pharmacol.* 2008;62(4):667-672. 4. Gronwald J, et al. *J Clin Oncol.* 2009;27(15S): Abstract 502.

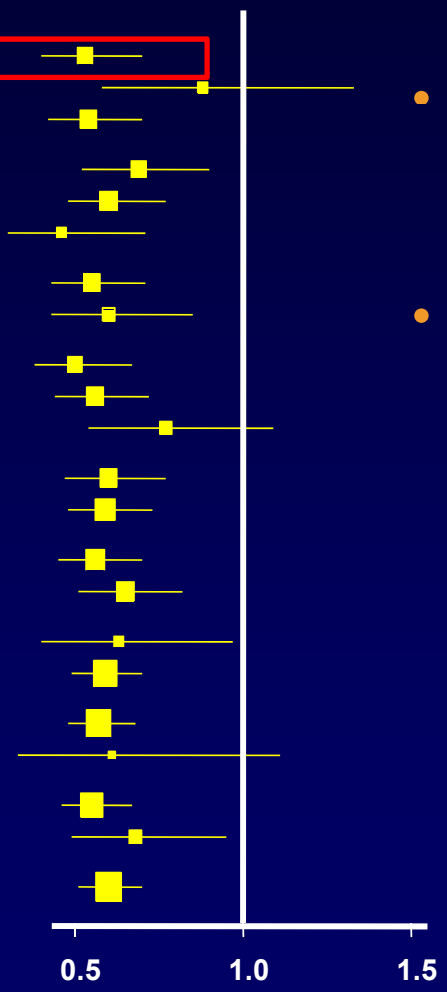
Anti-VEGF Therapy (Bevacizumab) in MBC

	E2100[1]		AVADO[2]		RIBBON-1: Capecitabine[3]		RIBBON-1: A/T[3]	
Placebo (Pl) controlled	No		Yes		Yes		Yes	
Chemotherapy	Weekly paclitaxel (P)		q 3 wk docetaxel (D)		Capecitabine (C)		q 3 wk docetaxel/*nab*PAC/ FAC/EC/FEC	
Dose of bevacizumab (B)	10 mg/kg q 2 wk		7.5 or 15 mg/kg q 3 wk		15 mg/kg q 3 wk		15 mg/kg q 3 wk	
	P	P+B	D+Pl	D+B	C+Pl	C+B	A/T+Pl	A/T+B
ORR	25%	49%	46%	55%/64%	24%	35%	38%	51%
PFS, months	5.9	11.8	8.1	9.0/10.0	5.7	8.6	8.0	9.2
HR	0.60 *P*<.0001		0.80 (7.5 mg) *P* = .0450 0.67 (15 mg) *P* = .0002		0.69 *P* = .0002		0.64 *P*<.0001	
OS, months	25.2	26.7	31.9	30.8/30.2	21.2	29	23.8	25.2
HR	0.88 *P* = .16		1.05 (7.5 mg) P= .72 1.03 (15 mg) P= .85		0.85 *P* = .27		1.03 *P* = .83	

1. Miller K, et al. *N Eng J Med.* 2007;357(26):2666-2676. 2. Miles DW, et al. *Cancer Res.* 2009;69(Suppl):Abstract 41.
3. Robert NJ, et al. *J Clin Oncol.* 2009;27(15S): Abstract 1005.

Antiangiogenic Benefit in Triple Negative

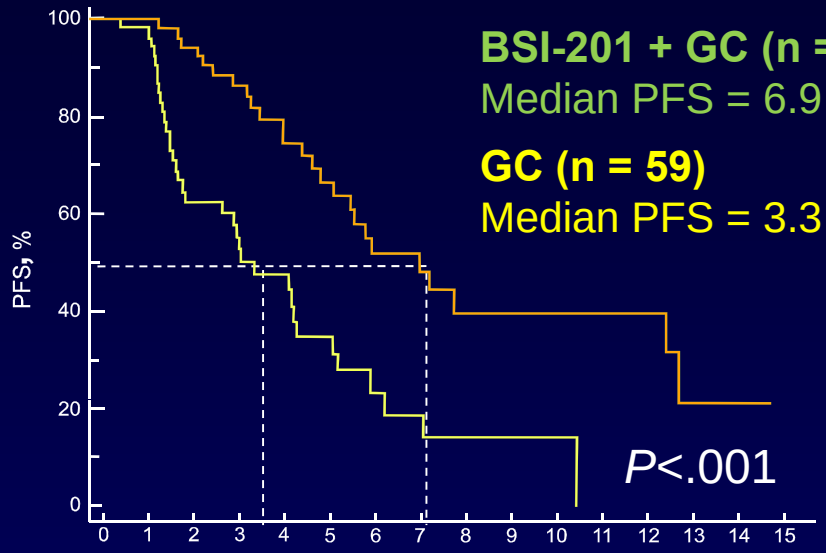
Group	N	HR	95% CI	PFS (mos) P	PFS (mos) P+B
ER-, PR-	233	**0.53**	(0.40, 0.70)	**4.6**	**8.8**
ER+, PR-	109	0.88	(0.58, 1.33)	9.3	12.6
ER+, PR+	289	0.54	(0.42, 0.70)	8.0	14.4
No adjuvant chemo	237	0.67	(0.51, 0.87)	6.5	13.6
Nontaxane	328	0.59	(0.47, 0.75)	7.7	10.8
Taxane	108	0.46	(0.30, 0.71)	3.0	12.0
Anthracycline	269	0.54	(0.42, 0.70)	5.6	10.7
Nonanthracycline	167	0.58	(0.42, 0.81)	8.0	13.2
Age 27 - 49	220	0.50	(0.38, 0.67)	5.5	12.5
Age 50 - 64	305	0.56	(0.44, 0.72)	6.7	11.3
Age 65 - 85	148	0.77	(0.54, 1.09)	7.9	11.9
DFI 0 - 24 months	277	0.60	(0.47, 0.77)	4.9	10.3
DFI > 24 months	396	0.59	(0.48, 0.73)	8.2	14.4
< 3 sites	373	0.56	(0.45, 0.70)	7.1	13.8
3 or more sites	300	0.65	(0.51, 0.82)	5.6	10.7
No visceral disease	113	0.63	(0.40, 0.97)	7.2	15.7
Visceral disease	560	0.59	(0.49, 0.70)	5.8	11.0
Not only bone	612	0.57	(0.48, 0.68)	5.7	11.3
Bone only	61	0.61	(0.33, 1.11)	13.0	19.7
Measurable	492	0.55	(0.46, 0.67)	5.6	11.2
Non-measurable	181	0.68	(0.49, 0.95)	11.4	13.9
Overall	**673**	**0.60**	**(0.51, 0.70)**	**5.9**	**11.8**



- **E2100: ER/PR- (HER2-) 47% improved DFS**
- **AVADO—similar findings**

Miller KD, et al. *N Engl J Med.* 2007;357(26):2666-2676.
Burstein HJ. et al, *J Clin Oncol.* 2008;26(11):1810-1816.

Phase II Gem/Carbo + IV PARP Inhibitor BSI-201 in Triple-Negative Breast Cancer (TNBC)



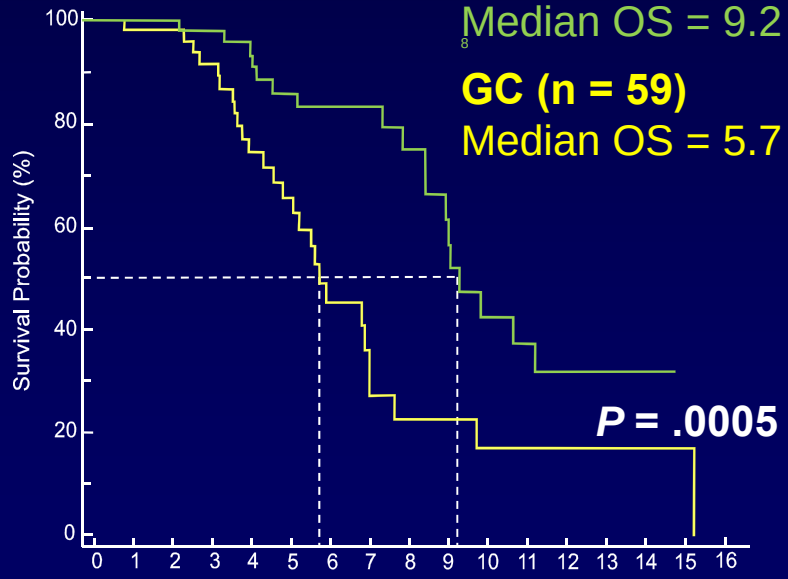
BSI-201 + GC (n = 57)
Median PFS = 6.9 months

GC (n = 59)
Median PFS = 3.3 months

PFS

BSI-201 + GC (n = 57)
Median OS = 9.2 months

GC (n = 59)
Median OS = 5.7 months



OS

PHASE III TRIAL OF THIS APPROACH – RESULTS LIKELY IN 2010

O'Shaughnessy J, et al. *J Clin Oncol.* 2009;27(18S): Abstract 3.

My Opinion

A clinical trial is the best answer…

Of the other choices, I would favor either combination chemotherapy, or chemotherapy with bevacizumab.