20th Multidisciplinary Management of Cancers: A Case-based Approach

Breast Tumor Board 2020

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20th Multidisciplinary Management of Cancers: A Case-based Approach

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20th Multidisciplinary Management of Cancers: A Case-based Approach
Case 1

- 59 y/o woman presents with left breast firmness in late summer 2019 which progresses to left nipple inversion by 10/2019.
- Exam and imaging consistent with a T4 N1 lesion.
- Biopsy reveals a grade 3 infiltrating ductal carcinoma, no in situ component; ER 0, PgR 0, HER2 0 and non-amplified.
- Punch biopsy of the left breast skin reveals dermal lymphatic involvement and core biopsy of a left axillary lymph node consistent with metastasis.

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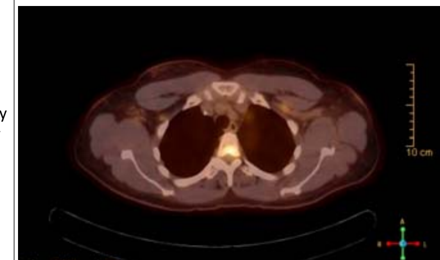
Case 1

- Imaging confirms T4 N1 lesion and a solitary suspicious lesion at T4; no biopsy is performed.
- Patient denies any bony symptoms.
- Plan is for neoadjuvant dose dense doxorubicin/cyclophosphamide (dd AC) followed by weekly paclitaxel and carboplatin, left mastectomy and radiation, and radiation to T4.



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Case 1
Do you recommend biopsy of T4?

1. Yes
2. No

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Case 1

- She initiates preoperative dd AC, seeks a 2nd opinion and transfers her care after C2.
- CT-guided biopsy confirms metastatic carcinoma, but insufficient tissue for hormone receptors, HER2 or PDL-1 staining.

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Case 1
With biopsy-proven metastatic disease, what chemotherapy do you recommend after dd AC?

1. Weekly paclitaxel x 12
2. Weekly paclitaxel x 12 + carboplatin
3. Weekly nab paclitaxel x 12 + atezolizumab
4. Weekly paclitaxel x 12 + carboplatin + atezolizumab

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Case 1

- She completes 11 of 12 weeks of paclitaxel in combination with carboplatin with an excellent response in the breast.
- She is seen by genetic counseling and found to harbor a *BRCA1* mutation.

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Case 1
What local therapy do you recommend?

1. None
2. Simple mastectomy + chest wall radiation
3. Mastectomy, ALND + chest wall radiation
4. Simple mastectomy + chest wall radiation + prophylactic BSO
5. Mastectomy, ALND + chest wall radiation + prophylactic BSO

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Case 1
Do you recommend radiation to T4?

1. Yes
2. No

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Case 1

- The patient undergoes left modified radical mastectomy with a residual 2.2 cm high-grade invasive mammary carcinoma with associated high-grade ductal carcinoma in situ. Dermal lymphatic involvement was present, but skin margins were negative. 5 lymph nodes were identified and 3 of these contained diffuse scattered individual tumor cells. Thus she had a residual yT2 N1 M1 left breast cancer.
- She receives chest wall XRT and radiation to T4.
- Post-treatment imaging reveals no disease.

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Case 1
What additional systemic therapy would you offer?

1. Nab-paclitaxel and atezolizumab
2. Capecitabine
3. Olaparib or talazoparib
4. No further therapy until disease progression

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Case 1: Key take home points

- Oligometastatic disease should be documented, but treated aggressively.
- Ongoing clinical trials in early and advanced TNBC to answer optimal (neo)adjuvant and local therapies

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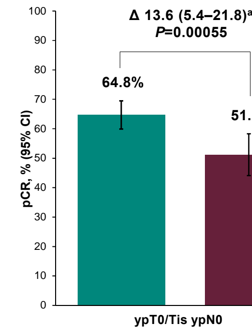
Definitive pCR Analysis



- Definitive pCR analysis to test primary hypothesis of pCR based on prespecified first 602 patients (pre-calculated P value boundary for significance of 0.003)
- Consistent benefit seen with pCR defined as ypT0 ypN0 and ypT0/Tis

Placebo + Chemo
Pembro + Chemo

Schmid, et al, SABCS 2019

[a]Estimated treatment difference based on Miettinen & Nurminen method stratified by randomization stratification factors. Data cutoff date: September 24, 2018.

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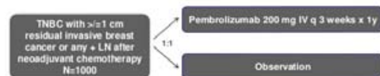
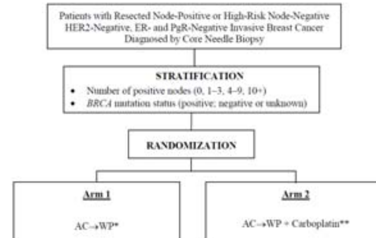
SWOG S1418/NRG BR006
RPhIII Pembrolizumab for Residual TNBC post NAC



NRG BR003



SWOG S1706

PhII olaparib during XRT for inflammatory breast cancer

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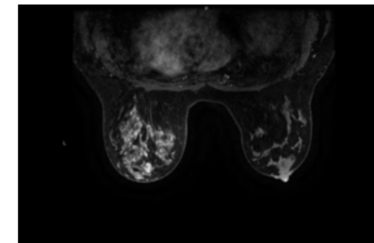
Case 2

- A 55 y/o woman presents with left breast pain.
- MMG and US reveal multiple left breast masses, ?left axillary adenopathy.
- Biopsy of the left breast reveals high grade DCIS, ER negative.
- Biopsy of axillary LN benign.



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Case 2

- The patient undergoes left nipple sparing mastectomy and SLN Bx revealing a 1.1 mm grade 2 IDC NOS and grade 3 DCIS, involving all quadrants. 2 sentinel LNs are benign and margins are negative.
- The invasive breast cancer stains ER 0, PgR 0 and HER2 3+/FISH amplified.

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Case 2
What adjuvant systemic therapy would you offer this T1A N0 tumor?

1. None
2. Weekly paclitaxel and a year of trastuzumab
3. Weekly paclitaxel and a year of trastuzumab + pertuzumab
4. Docetaxel, carboplatin and a year of trastuzumab
5. Docetaxel, carboplatin and a year of trastuzumab + pertuzumab

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Case 2
What if the tumor were hormone receptor positive?

1. Endocrine therapy
2. Endocrine therapy + a year of trastuzumab
3. Chemotherapy → endocrine therapy + a year of trastuzumab

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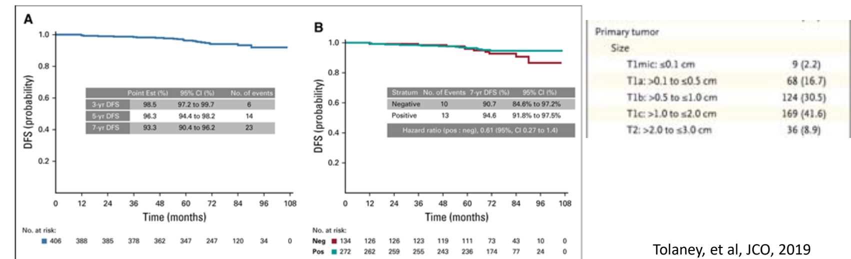
Case 2



Tolaney, et al, JCO, 2019

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Case 2: Key take home points

- No randomized trials on T1A/B N0 HER2+ tumors
- APT phase II trial shows DFS and OS outcomes are excellent
- ATEMPT trial

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Case 3

- 60 y/o has a clinical T2 N0 right breast mass on screening mammogram.
- Core biopsy reveals a grade 2 IDC, ER 80%, PgR 20%, HER2 3+/FISH amplified.
- She receives 6 cycles of neoadjuvant docetaxel, carboplatin, trastuzumab and pertuzumab (TCHP).
- She undergoes right lumpectomy and SLN Bx revealing minimal residual IDC, “small nests of IDC totaling < 1mm” with areas of cytologic atypia and sclerosis, “consistent with treatment effect”.

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Case 3
In addition to endocrine therapy and post lumpectomy XRT, what HER2-directed therapy do you recommend?

1. TDM-1 x 14 cycles
2. Trastuzumab to complete a year
3. Trastuzumab and pertzumab to complete a year

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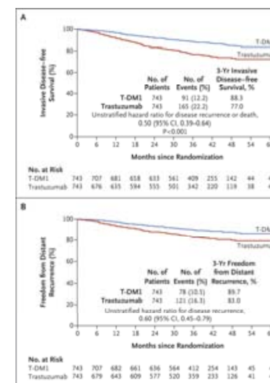
Case 3



- ypT1a, ypT1b or ypT1mic and ypN0 (at definitive surgery) = 20%

Von Minckwitz, et al, NEJM 2019

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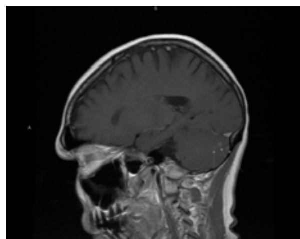
Case 3

- The patient opts to take trastuzumab and pertuzumab and completes a year.
- Two months after completion, a brain MRI reveals multiple supra-and infratentorial nodules, consistent with metastatic disease.
- Imaging reveals no disease outside the CNS.
- She completes gamma knife therapy.



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Case 3
Regarding systemic therapy, what do you recommend?

1. Taxane + trastuzumab and pertuzumab
2. Change in endocrine therapy + trastuzumab and pertuzumab
3. TDM-1
4. Trastuzumab-deruxtecan
5. Tucatinib

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Case 3: Key take home points

- There are options for adjuvant TDM-1 for residual disease, adjuvant pertuzumab for “high” risk disease.
- The CNS remains a high risk site for metastatic HER2 positive disease.
- Trastuzumab deruxtecan was FDA approved on December 20, 2020 for patients who have received $\geq$2 HER2 directed therapies in the metastatic setting.
- Tucatinib was FDA approved on April 17, 2020, in combination with capecitabine and trastuzumab in pateints who have received 1 prior HER2-directed therapy in the metastatic setting.

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Case 4

- A 55 y/o woman, with developmental delay, presents with a left locally advanced breast cancer 2-3 years after first noticing a left breast mass. Biopsy reveals a grade 2 infiltrating ductal carcinoma, ER 95%, PgR 95% and HER2 negative.
- Imaging shows no distant metastases. Breast MRI demonstrates a large left breast mass with skin and pectoralis major involvement and suspicious left axillary adenopathy.
- She receives dd AC followed by dd paclitaxel with a partial response.
- Post-treatment breast MRI reveals a 4.7 cm mass with involvement of the pectoralis and resolved left axillary adenopathy.

- She is felt to be unresectable by her local surgeon and placed on endocrine therapy.
- She is referred to UC Davis for further local therapy. On exam, she had a 5 cm, firm left breast mass and no axillary adenopathy.

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Case 4

What initial local therapy do you recommend?

1. Left mastectomy and SLN Bx
2. Left mastectomy and ALND
3. Left breast radiation, then consideration of mastectomy
4. Left breast radiation
5. No local therapy; further systemic therapy

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Case 4

Subtype (N)	pCR = RCB 0 (%)	RCB 1 (%)
HR-, HER2- (1774)	43	12
HR-, HER2+ (572)	69	11
HR+, HER2+ (858)	38	20
HR+, HER2- (1957)	11	11

Symmans, et al, SABCS 2019

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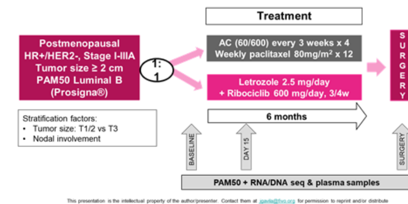
Case 4

CORALLEEN trial Design



	Chemotherapy n= 52		Ribociclib + letrozole n= 49	
	N (%)	95% CI	N (%)	95% CI
ROR-low	24 (46.1%)	32.9-61.5	23 (46.9%)	32.5-61.7
ROR-intermediate	16 (30.8%)	19.1-45.9	15 (30.6%)	18.2-45.4
ROR-high	11 (21.2%)	11.2-35.2	11 (22.5%)	11.8-36.7
Missing	1 (1.9%)	NA	NA	NA

Gavila, et al, SABCS 2019;
Prat, et al, Lancet Onc, 2020

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Case 4: Key take home points

- Local therapy after a poor response to neoadjuvant chemotherapy remains a challenge.
- Consider preoperative endocrine therapy in select patients.
- The use of CD 4/6 kinase inhibitors outside the metastatic setting is investigational.

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Case 5

- A 48 y/o woman undergoes a right mastectomy and SLNBx after presenting with a palpable mass.
- Pathology reveals a multifocal, grade 2, invasive mammary carcinoma with aprocrine and mucinous features of 2.1 cm and 1.2 cm. There is grade 2 DCIS of 4 cm. Margins are negative. Both tumors are ER+ (100%), PgR+ (90%) and HER2 negative.
- She had an anatomic stage IIA, clinical prognostic stage IB, T2 N0, right breast cancer.
- Oncotype Dx assays reveal:
  - 2.1 cm tumor: RS 16
  - 1.2 cm tumor: RS 18

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Case 5
What adjuvant therapy do you recommend?

1. Chemotherapy followed by endocrine therapy
2. Endocrine therapy alone

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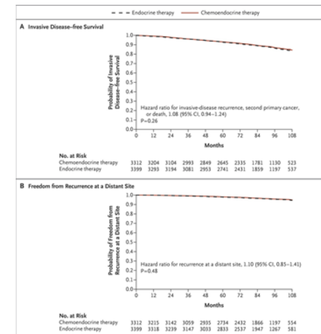
Case 5



Freedom from recurrence of breast cancer at a distant site		
Score of ≤10, endocrine therapy	99.7±0.3	98.5±0.8
Score of 11–15, endocrine therapy	98.8±0.6	97.2±1.0
Score of 11–15, chemoendocrine therapy	98.5±0.7	98.0±0.8
Score of 16–20, endocrine therapy	98.1±0.7	93.6±1.4
Score of 16–20, chemoendocrine therapy	98.9±0.5	95.2±1.3
Score of 21–25, endocrine therapy	93.2±1.7	86.9±2.9
Score of 21–25, chemoendocrine therapy	96.4±1.2	93.4±2.3
Score of ≥26, chemoendocrine therapy	91.1±1.6	88.7±2.1
Freedom from recurrence of breast cancer at a distant or local–regional site		
Score of ≤10, endocrine therapy	98.4±0.6	95.4±1.3
Score of 11–15, endocrine therapy	97.5±0.8	93.3±1.6
Score of 11–15, chemoendocrine therapy	97.2±0.9	94.4±1.5
Score of 16–20, endocrine therapy	95.7±1.0	89.6±1.9
Score of 16–20, chemoendocrine therapy	97.2±0.8	93.0±1.5
Score of 21–25, endocrine therapy	89.8±2.0	82.0±3.2
Score of 21–25, chemoendocrine therapy	94.2±1.6	90.7±2.5
Score of ≥26, chemoendocrine therapy	88.6±1.8	86.1±2.2
Overall survival		
Score of ≤10, endocrine therapy	100.0	98.6±0.9
Score of 11–15, endocrine therapy	99.3±0.4	96.8±1.0
Score of 11–15, chemoendocrine therapy	98.9±0.6	97.5±0.9
Score of 16–20, endocrine therapy	98.6±0.6	95.8±1.2
Score of 16–20, chemoendocrine therapy	99.8±0.2	96.1±1.2
Score of 21–25, endocrine therapy	98.2±0.9	92.7±2.0
Score of 21–25, chemoendocrine therapy	98.3±0.8	93.9±1.9
Score of ≥26, chemoendocrine therapy	95.6±1.1	92.4±1.9

Sparano, et al, NEJM 2018

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Case 5
What type of endocrine therapy do you recommend? Duration?

1. Tamoxifen
2. Tamoxifen + Ovarian Suppression (OS)
3. Aromatase inhibitor + OS

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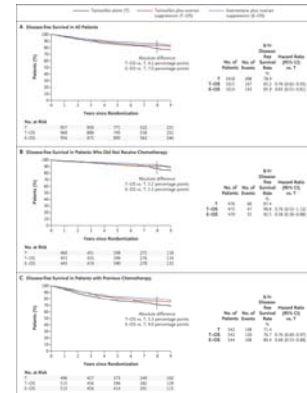
Case 5



Francis, et al, NEJM 2018

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Case 5: Key take home points

1. Gene expression assays can identify patients who may not benefit from adjuvant chemotherapy, but there remain questions of benefit in premenopausal women.
2. Optimal endocrine therapy and duration of therapy continues to evolve for premenopausal women.

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Thanks to the audience and our panel!

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