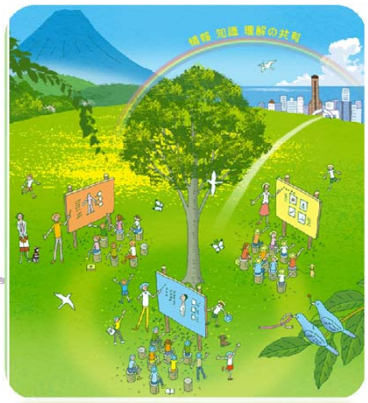
中部乳がん会議

2013年３月２-３日 (土-日　曜日)

① 君たちに伝えたいこと
② St.Gallen 直前情報

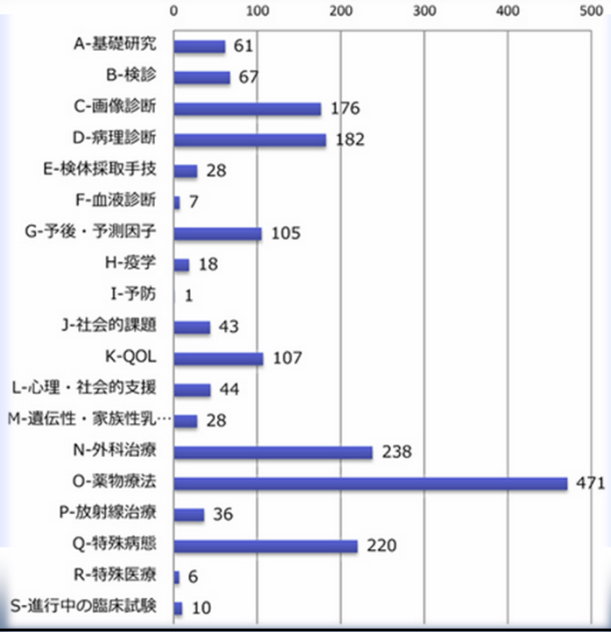


浜松オンコロジーセンター
腫瘍内科　渡辺　亨
twatanab@oncoloplan.com

君たちにつたえたいこと

- サイエンス、エビデンスを尊重する心をもってほしい
- 日々の診療に埋没せず研究にとりくんでほしい
- 若い時代の貴重な時間を切り売りしないほうがよい
- 寝食を忘れて研究に打ち込んでほしい
- 親はなくとも子は育つ　子供の行事は過剰重視しない
- 時代についていくのではなく時代をリードしてほしい
- 科学的、倫理的な乳がん診療を実践してほしい
- ワーク・ライフ・スタディ　バランスを意識してほしい

第２１回日本乳癌学会総会
カテゴリー別　応募演題数



第２１回日本乳癌学会総会
応募演題の特徴

応募総数	1850	
		%
少数例報告	394	21.3
前向き臨床試験	5	0.2
非採択	71	3.8

まちがった取り組み

プレジデンシャルシンポジウムのテーマに合わせて演題をとりつくろう

K先生の指摘
「プレジデンシャルシンポジウムがなければ演題の出しようがありませんからね

きっと演題は減るんじゃないですか

毎年、プレジデンシャルシンポジウムの最後の方でしょうもない発表をしているK先生

乳癌学会の演題募集が始まってからテーマを決めてカルテ調査を始める

トリネガ症例の家族歴調べて遺伝性乳がんの頻度とかの検討にしてみるか？

正しい取り組み

- **3年先の稽古をする**
  毎年、1月の最初のカンファレンスで
  「再来年の乳癌学会 癌治療学会 ASCO SanAntonio などの学会に出す演題の研究テーマを検討する」
- **計画性を持ち前向きに取り組む**
- **チームリーダーの責任においてこれを成す**

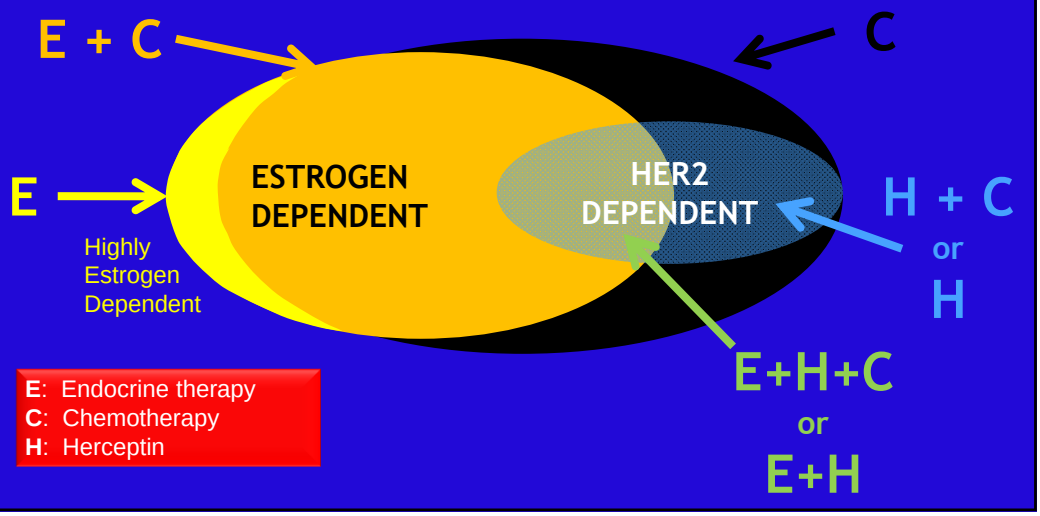
がん治療　20世紀から21世紀へ

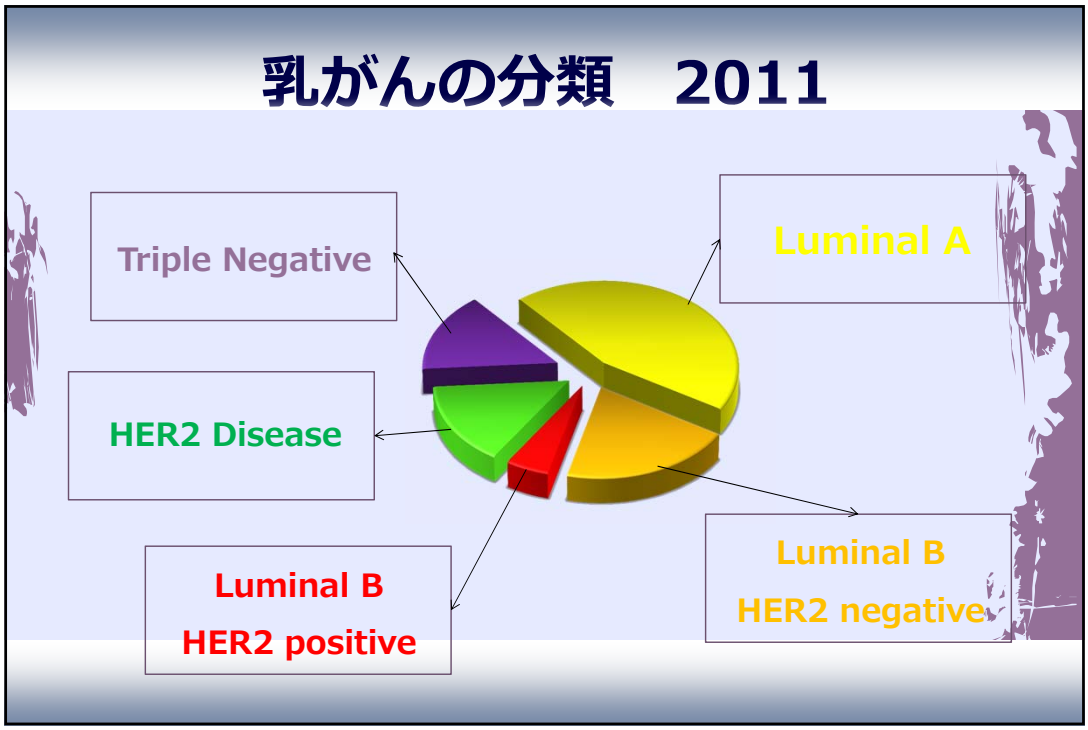
集団的・集団治療 → すべての転移性乳がん患者に
ADM＋CPA+TAM
5′ DFUR+CPA+MPA

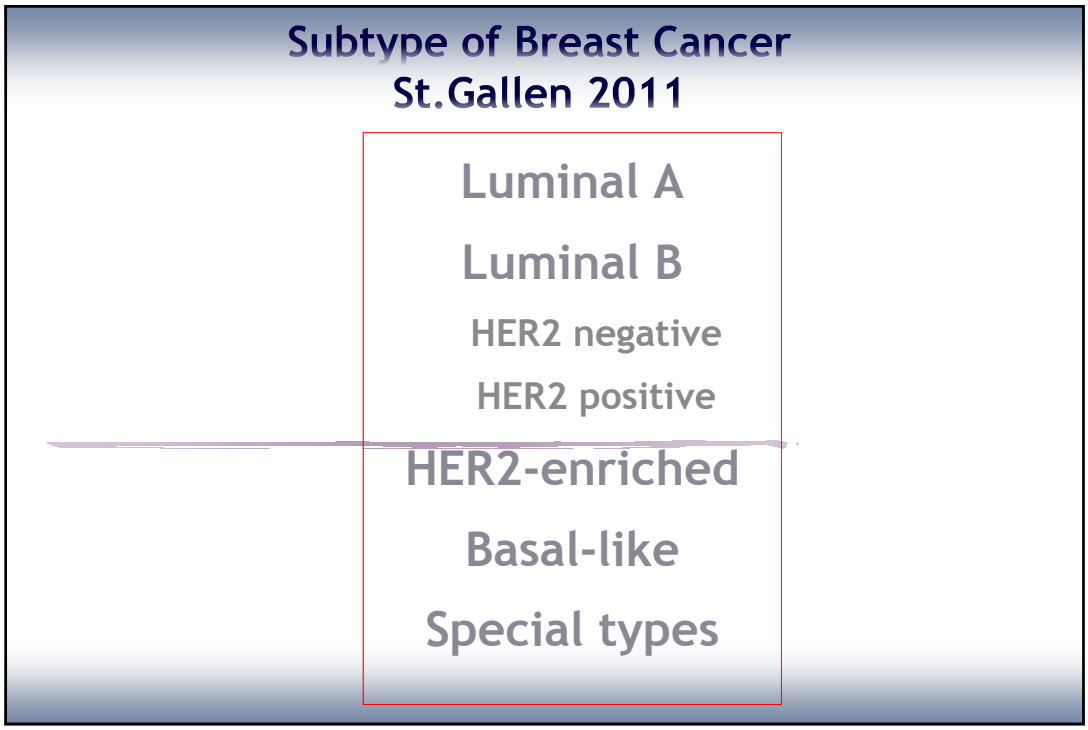
個別的・集団治療 → n (-) には　AC
n (+) には　AC→paclitaxel

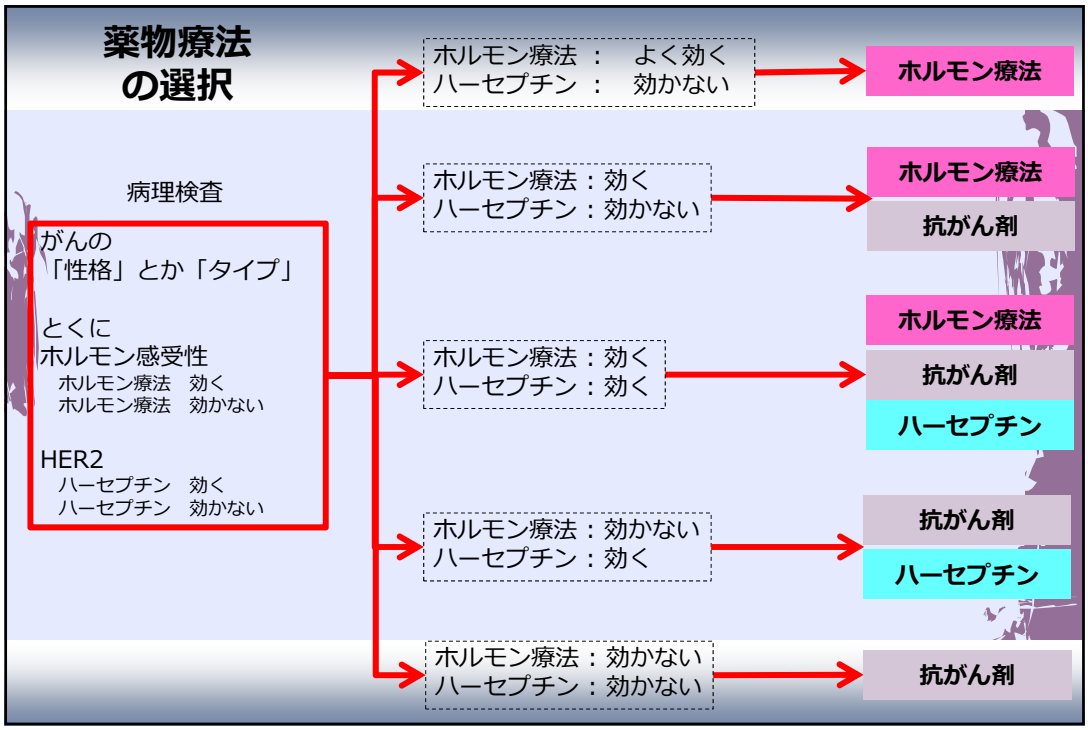
個別的・準個別治療 → ER (+) には　ホルモン剤
HER2 (+) には　抗HER2剤

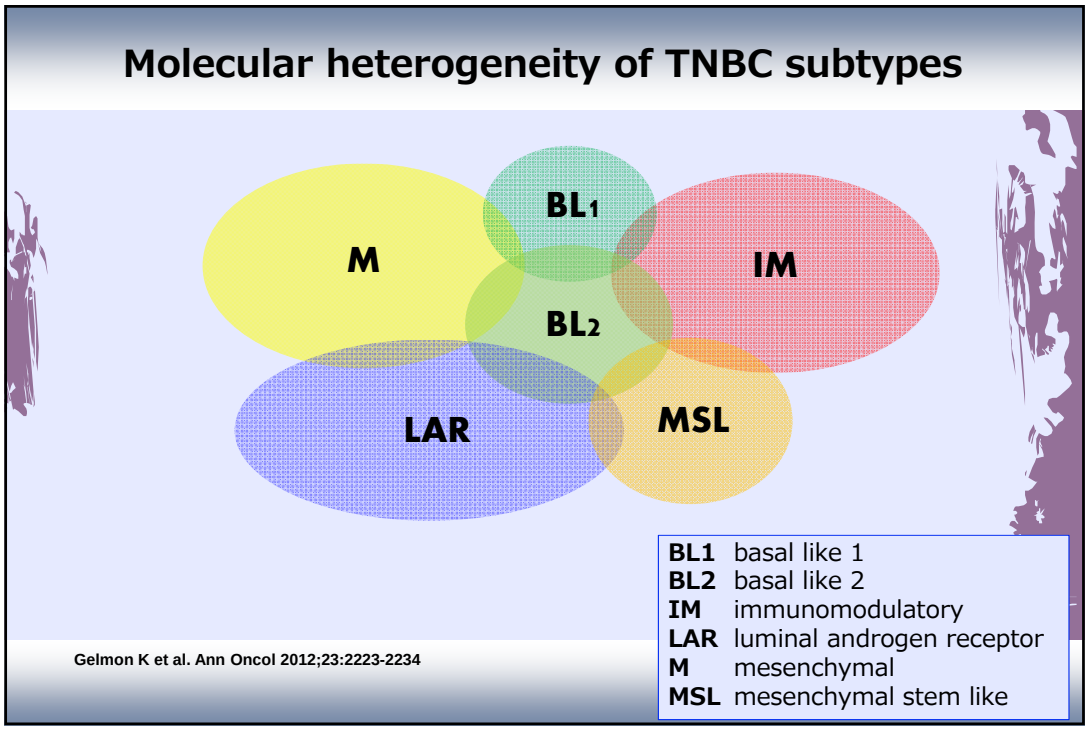
Tailored Treatment of Breast Cancer started in 1990's

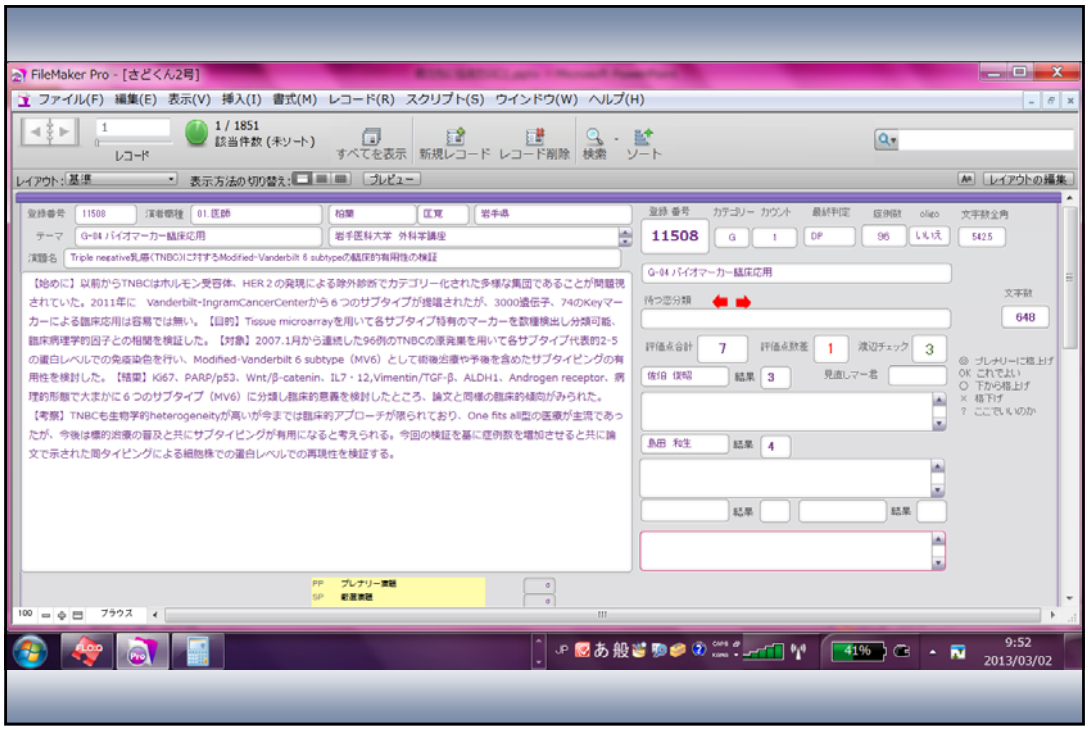



乳がんの分類　2011
Triple Negative
Luminal A
HER2 Disease
Luminal B
HER2 negative
Luminal B
HER2 positive


Subtype of Breast Cancer
St.Gallen 2011
Luminal A
Luminal B
HER2 negative
HER2 positive
HER2-enriched
Basal-like
Special types


薬物療法の選択
病理検査
がんの「性格」とか「タイプ」
とくに
ホルモン感受性
ホルモン療法　効く
ホルモン療法　効かない
HER2
ハーセプチン　効く
ハーセプチン　効かない
ホルモン療法 ： よく効く
ハーセプチン ： 効かない
ホルモン療法
ホルモン療法：効く
ハーセプチン：効かない
ホルモン療法
抗がん剤
ホルモン療法：効く
ハーセプチン：効く
ホルモン療法
抗がん剤
ハーセプチン
ホルモン療法：効かない
ハーセプチン：効く
抗がん剤
ハーセプチン
ホルモン療法：効かない
ハーセプチン：効かない
抗がん剤


Molecular heterogeneity of TNBC subtypes
BL1
M
IM
BL2
LAR
MSL
BL1 basal like 1
BL2 basal like 2
IM immunomodulatory
LAR luminal androgen receptor
M mesenchymal
MSL mesenchymal stem like
Gelmon K et al. Ann Oncol 2012;23:2223-2234



遺伝子異常の発見と治療薬の開発

異常遺伝子	発見年	疾患	治療薬	国際誕生	日本承認
BCR-ABL 転座	1973	慢性骨髄性白血病	イマチニブ	2001	2005
HER2増幅	1985	乳癌	トラスツズマブ	1998	2001
KRAS野生型	1987	結腸癌	パニツムマブ	2006	2010
PML-RARA 転座	1990	急性骨髄性白血病	トレチノイン	1987	1995
BRAF V600変異	2001	悪性黒色腫	ヴェムラフェニブ	2011	not yet
KIT変異	2001	消化管間質腫瘍	イマチニブ	2001	2005
EGFR変異	2004	非小細胞肺癌	ゲフィチニブ	2002	2002
ALK融合遺伝子	2007	非小細胞肺癌	クリゾチニブ	2010	2012

個別的・個別治療の商業化

Oncotype Dx

MammaPrint

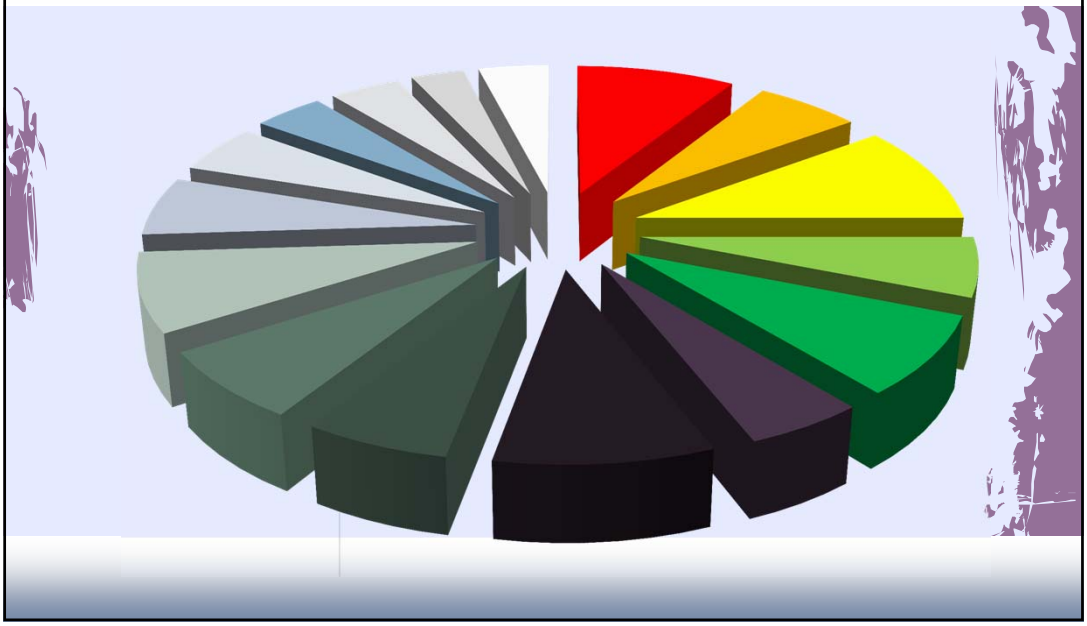
PAM 50

Endopredict

Epclin

・
・
・

乳がんのサブタイプ　20XX



T1aN0M0 stage I Luminal A

39才　女性

- 中学校教員
- 23歳で結婚　16年間、何回か不妊症治療に取り組んだが妊娠せず

- 経過

5年前　　左D領域腫瘤→　切開生検　→　鑑別困難　→　経過観察
半年前　　創部近くに腫瘤　→　針生検　→　鑑別困難
1か月前　　JTD大学受診　→　CNB　→　乳癌と診断 →　GKARAK病院へ転院希望

今月　　GKARAK病院　→　左 Bt + Ax (level 2)
【病理】 a3>a2 n=1/29 t=0.9cm ER (AS 8) PgR (AS 8) HER2 0 grade 1

挙児希望あり
討論
- 受精卵凍結保存など、挙児対策をどうするか？
- 薬物療法の選択はどうするか？




本日の話題メニュー

話題番号	今日の話
1	豊かな国 日本に暮らす幸せ アバスチンのエビデンスを考える
2	乳がん個別化医療 確かに進歩しているようだが・・
3	ピンクリボンキャンペーンの終焉
4	**St.Gallen 2013**

St. Gallen 2013

Rational Recommendations – Personalizing the Approach to Treatment of Women with Early Breast Cancer

Consensus & Controversy

St. Gallen 2013

- Introduction of the Panel
- Introduction of the Process
- Key areas of Controversy
  - Aim: majority, opinion-based consensus on practical issues

International Consensus Panel - 2013 St.Gallen

Eric P. Winer, USA & Aron Goldhirsch, CH/I (Chairmen)

- *Kathy Albain (USA)*
- *Fabrice André (F)*
- *José Baselga (USA)*
- *Jonas Bergh (S)*
- *Hervé Bonnefoi (F)*
- *Denisse Bretel-Morales (PE)*
- *Harold J. Burstein (USA)*
- *Fatima Cardoso (P)*
- *Monica Castiglione Gertsch (CH)*
- *Alan S. Coates (AUS)*
- *Marco Colleoni (I)*
- *Alberto Costa (I)*
- *Giuseppe Curigliano (I)*
- *Nancy Davidson (USA)*
- *Angelo Di Leo (I)*
- *Bent Ejlertsen (DK)*
- *John F. Forbes (AUS)*
- *Richard D. Gelber (USA)*
- *Michael Gnant (A)*
- *Pamela J. Goodwin (CAN)*
- *Paul E. Goss (USA)*
- *Jay R. Harris (USA)*
- *Daniel F. Hayes (USA)*
- *Clifford A. Hudis (USA)*
- *James N. Ingle (USA)*
- *Jacek Jassem (PL)*
- *Zefei Jiang (CN)*
- *Per Karlsson (S)*
- *Sibylle Loibl (D)*
- *Monica Morrow (USA)*
- *Moise Namer (F)*
- *C. Kent Osborne (USA)*
- *Ann H. Partridge (USA)*
- *Frédérique Penault-Llorca (F)*
- *Charles M. Perou (USA)*
- *Martine Piccart-Gebhart (B)*
- *Kurt Possinger (D)*
- *Kathleen I. Pritchard (CAN)*
- *Emiel J.T. Rutgers (NL)*
- *Felix Sedlmayer (A)*
- *Vladimir Semiglazov (RUS)*
- *Zhi-Ming Shao (CN)*
- *Ian Smith (UK)*
- *Beat Thürlimann (CH)*
- *Masakazu Toi (JPN)*
- *Andrew Tutt (UK)*
- *Michael Untch (D)*
- *Giuseppe Viale (I)*
- *Toru Watanabe (JPN)*
- *Nicholas Wilcken (AUS)*
- *William C. Wood (USA)*

Areas of Controversy - Need for Debate

- Controversies deserve:
  - Debate leading to a consensus
  - Debate leading to a range of resolutions (because different approaches are needed in different environments / countries)
  - Debate defining need for further trial(s)
- Areas which do not require discussion because evidence is accepted by most / all

Areas of Controversy - Need for Debate

- Clinical trials are…
  - … useful for defining whether one treatment is better than another in a "defined population"
  - … useful for defining the average improvement in treatment outcome
  - … do not always define how to treat an individual patient
- Using available evidence to decide treatment for an individual patient involves interpretation and debate

Primary Consideration
(agreed on by Majority of Participants)

- Primary goal - treatment choice for women with early breast cancer:
  - utilize tumor biology to determine responsiveness to various treatments;
  - utilize tumor extent to estimate level of benefit justifying treatment for the individual patient;
  - utilize these plus estimates of the risks of therapy and patient preference to define preferred management.
    - Guidelines should be provided to patients in appropriate language and format to assist decision-making and optimize informed consent
    - Patient preference, assuming that the options are understood, is paramount and may lead to adjustment in treatment

Questions

- … should be unambiguous and not directive
- … should lead to the best recommendations outside of clinical trials. Alternatives for less well-resourced areas/countries should be identified if the treatment is less costly and only marginally less effective.
- Refer to usual histologic types (special subtypes require separate consideration)
- Exclude the treatment of pregnant paitents as well as those with significant co-morbidities
- Age cut-off for “young” may depend on question

Panelists' Answers

- Questions have been prospectively reviewed by the Panelists and revised to be as clear as possible. Further semantics discouraged!!
- Therefore, Panelists are asked to answer

  Yes or No

  recognizing that some uncertainty may exist.
- Abstain (A) for insufficient data, not an expert on the issue, or conflict of interest.

Key Areas of Controversy

- Surgery of the primary
- Surgery of the axilla
- Radiation: partial breast, post-mastectomy, nodal areas, advanced technologies
- Pathology: Ki-67, ER, HER2, grade, other markers
- Multi-gene signatures: 21 gene RS, PAM-50, 70 gene signature, EPClin, other
- Stroma: extracellular matrix and prognosis
- Endocrine therapies: ovarian suppression, tamoxifen, AI
- Chemotherapies: luminal A, duration, regimen
- Anti-HER2 therapies: combination, duration
- Neo-adjuvant systemic therapy
- Bisphosphonates: anti-tumor effects
- Follow up after early breast cancer

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Surgery

Surgery Issues
(Summary Slide)

- Assessment of tumor extent to decide:
  - mastectomy
  - breast conservation
  - neoadjuvant chemotherapy
- In case of breast conservation:
  - sufficient cytoreduction for optimal in-breast cancer control
  - optimal strategies for cosmesis
- Indications for sentinel node procedure
- Indications for full axillary clearance

Surgery of the Primary

When considering breast conserving surgery the following factors are contraindications

- Young age (<35 yr)

Relative	Yes	No	A
Absolute	Yes	No	A

- Young age (< 40 yr)

Relative	Yes	No	A
Absolute	Yes	No	A

- Extensive or diffuse microcalcification

Relative	Yes	No	A
Absolute	Yes	No	A

Surgery of the Primary

When considering breast conserving surgery the following factors are contraindications

- Multi-focal disease
  - Relative Yes No A
  - Absolute Yes No A
- Multi-centric disease
  - Relative Yes No A
  - Absolute Yes No A
- Tumour close to nipple
  - Relative Yes No A
  - Absolute Yes No A

Surgery of the Primary

When considering breast conserving surgery the following factors are contraindications

- Extensive vascular invasion
  - Relative Yes No A
  - Absolute Yes No A
- Extens. intraductal component
  - Relative Yes No A
  - Absolute Yes No A
- Lobular histology
  - Relative Yes No A
  - Absolute Yes No A

Surgery of the Primary

When considering breast conserving surgery the following factors are relative contraindications:

- Family history Yes No A
- BRCA1 positivity Yes No A
- BRCA2 positivity Yes No A
- Involved margins after repeated excisions (including DCIS)
  Yes No A
- Unfavourable biology on gene expression/sequencing
  Yes No A
- Contraindications to breast irradiation that should follow breast conserving surgery
  Yes No A

Surgery of the Primary

Is skin-nipple sparing mastectomy an acceptable treatment without RT?

Yes No A

ONLY if margin toward nipple is tumour-free and immediate reconstruction planned

Yes No A

Surgery of the Primary

- Should MRI be routine for patients with newly diagnosed disease (to assist decision on BCS)?

  Yes No A

- In women undergoing breast conserving surgery the minimum appropriate surgical margin is
  - No ink on invasive tumor? Yes No A
  - 1 mm clearance (invasive)? Yes No A
  - 3 mm clearance (invasive)? Yes No A
  - 5 mm clearance (invasive)? Yes No A
  - 2 mm clearance (DCIS)? Yes No A
  - Dependent on tumor biology? Yes No A

Surgery of the Axilla

In patients with macrometastases in 1-2 sentinel nodes, completion axillary dissection can safely be omitted following:

- Mastectomy (no radiotherapy planned)

  Yes No A

- Mastectomy (radiotherapy planned)

  Yes No A

- Conservative resection and radiotherapy

  Yes No A

Surgery of the Axilla

In patients otherwise undergoing breast conserving surgery, completion axillary dissection is necessary if :

- Clinical N1 ? Yes No A
- 3 or more positive SLNs? Yes No A
- Nodal status (eg. N 4+) needed for chemotherapy choice? Yes No A

Radiotherapy

Radiotherapy Issues

(Summary Slide)

- Subgroup that does not need any RT?
- Subgroup suitable for partial breast RT?
- Risk factors requiring post-mastectomy RT to chest wall?
- Indications for RT axilla; SCF; internal mammary chain?
- 15- and 16-fraction schedules for whole breast RT?
- Tumour bed boost dose needed in women >50 with complete microscopic resection margins?

RT: Conserved Breast Irradiation

- Is there a group not requiring RT as part of BCT?

  Yes No A
- Should «short course» RT (e.g. 40 Gy in 15 fractions) be offered as a standard?

  Yes No A
- Is «short course» RT as above an option if boost is also planned?

  Yes No A

RT: Partial Breast Irradiation

Following breast conserving surgery, partial breast irradiation may be used:

- As the definitive irradiation, without any external beam therapy (ASTRO/ESTRO group)?

  Yes No A
- Only in the absence of adverse tumor pathology?

  Yes No A
- Intra-operatively?

  Yes No A
- Replacing a boost in the context of whole breast external beam irradiation?

  Yes No A

Radiation Therapy: After Mx

Should post Mx RT be standard for patients with:

- N+ ≥4? Yes No A
- N+ 1 to 3: all patients? Yes No A
- N+ 1 to 3 with adverse pathology? Yes No A
- N+ 1 to 3 at young age (< 40 yr)? Yes No A
- pN0 after axillary dissection but < 8 nodes examined? Yes No A
- Positive sentinel node biopsy but no axillary dissection? Yes No A

Radiation Therapy: After Mx

Should post Mx RT be standard for patients with:

- Young age (< 40 yr) regardless of nodes? Yes No A
- Adverse pathology regardless of nodes?
  - Grade 3 Yes No A
  - Lymphovascular invasion Yes No A
  - HER2+ Yes No A
  - Triple negative Yes No A
- T > 5 cm regardless of nodes? Yes No A
- Positive deep/radial margins? Yes No A

Radiation Therapy

Nodal areas requiring irradiation should:

- Include SCF in all irradiated patients? Yes No A
- Include axilla in all irradiated patients? Yes No A
- Include IMN in all irradiated patients? Yes No A
- Be influenced by response to neoadjuvant therapy? Yes No A
- Avoid the axilla following standard surgical dissection? Yes No A
- Be influenced by the intrinsic subtype of the tumor? Yes No A

Pathology

Pathology

For practical purposes, distinction between ‘Luminal A’ and ‘Luminal B’ (Her2 Neg) tumors can be:

- made by ER, PR alone? Yes No A
- made by ER, PR and Ki-67? Yes No A
- made with grade 3 as a substitute for high Ki-67? Yes No A
- only safely determined by molecular diagnostics? Yes No A
- only safely determined by laboratories participating in quality assurance programs? Yes No A

Pathology: HER2

In the determination of HER2 status for anti-HER2 treatment purposes, do we need to know:

- Heterogeneity of overexpression of HER2?
  Yes No A
- Polysomy 17
  Yes No A

For treatment decisions do we also need to know

- Concomitant estrogen receptor expression status?
  Yes No A
- Degree of tumor proliferation?
  Yes No A

Pathology: Subtypes

- Intrinsic subtypes may influence whether or not chemotherapy is used in the adjuvant regimen?
  Yes No A
  - If yes, multi-gene expression array profiling is required for subtype definition?
    Yes No A
  - Yes, but clinicopathologic definition of 'subtype' (e.g. St Gallen 2011) is sufficient for this purpose?
    Yes No A
- Choice of cytotoxic therapy regimen should be influenced by intrinsic subtype?
  Yes No A

Multi-Gene Signatures

Would you ask for one of the multigene signatures (after clinicopathological assessment) :

- in nearly all cases independently of the 'intrinsic subtype'?
  Yes No A
- in nearly all ER and/or PgR positive ' (HER2-neg) cases?
  Yes No A
- in nearly all 'Luminal B' (HER2-neg) but not 'Luminal A' cases?
  Yes No A
- in N-neg. ER positive ' (HER2-neg) cases?
  Yes No A
- in N-pos. ER positive ' (HER2-neg) cases?
  Yes No A

Multi-Gene Signatures

In an endocrine-responsive* cohort:

- Does 21 gene RS predict Chemotherapy (ChT) response?
  Yes No A
- Does PAM-50 predict ChT response?
  Yes No A
- Does 70 gene signature predict ChT response?
  Yes No A
- Does EPClin predict ChT response?
  Yes No A

* i.e. any expression of ER and/or PgR

Multi-Gene Signatures

In an endocrine-responsive cohort*, selection of patients who might forego chemotherapy can be partially based on:

- 21 gene RS
  Yes No A
- PAM-50
  Yes No A
- 70 gene signature
  Yes No A
- EPClin
  Yes No A

* i.e. any expression of ER and/or PgR

Molecular Diagnostics

- In an endocrine-responsive cohort*, molecular diagnostics can be omitted if:
- Chemotherapy would not be given anyway because:
  - T size ≤ 1 cm? Yes No A
- Chemotherapy would be given anyway because:
  - T size (e.g. > 5 cm)? Yes No A
  - Inflammatory BC? Yes No A
  - 1-3 nodes+? Yes No A
  - ≥ 4 nodes+? Yes No A
  - Grade 3? Yes No A
  - Low ER% (e.g. 5%) Yes No A
  - Young age (e.g.< 35) Yes No A

* i.e. any expression of ER and/or PgR

Stroma

Stroma

Pathological features of the stroma which should influence therapy choice in routine clinical practice include:

- Immunocyte infiltration? Yes No A
- Microvascular density? Yes No A
- Stromal p16 staining? Yes No A
- Other? Yes No A

Endocrine Therapies

Endocrine Therapy:
Establishing Standards for Premenopausal

- Tam alone as default? Yes No A
- Tamoxifen duration should be extended to 10 years in patients remaining premenopausal?
  Yes No A
- Ovarian function suppression (OFS) should be added to Tam:
  - In all patients Yes No A
  - In the young (e.g. < 40 yr)
    Yes No A

Endocrine Therapy:
Establishing Standards for Premenopausal

- OFS alone (without tamoxifen) ?
  Yes No A
- AI + OFS is a valid option in case of contraindicated tam?
  Yes No A
- AI + OFS is a valid option in all patients?
  Yes No A

Endocrine Therapy:
Establishing Standards for Postmenopausal

- Can some patients be adequately treated with tamoxifen alone?
  Yes No A
- If an AI, need it be started upfront in all patients?
  Yes No A
- If an AI, need it be started upfront in high risk?
  Yes No A
- Can upfront AI be replaced with TAM after 2 yr?
  Yes No A

Endocrine Therapy:
Establishing Standards for Postmenopausal

- Should extended AI beyond 5 years of adjuvant endocrine treatment be offered to patients with:
  - node-positive disease? Yes No A
  - node-negative disease? Yes No A
- If so, does the prior endocrine therapy matter?
  Should extended AI beyond 5 years be given after
  - 5 years adjuvant tamoxifen? Yes No A
  - 5 years endocrine therapy switching from tamoxifen to an AI? Yes No A
  - 5 years adjuvant AI? Yes No A
- If AI is unavailable or not tolerated, (so that patient has switched to tamoxifen), should tamoxifen be continued beyond 5 years? Yes No A

Chemotherapies

Chemotherapy
Basic Questions

Factors arguing for inclusion of ChT are:

- Histological grade 3 tumor ? Yes No A
- Ki-67 high Yes No A
- Low hormone receptor status? Yes No A
- Positive HER2 status? Yes No A
- Triple negative status? Yes No A

Chemotherapy
Basic Questions

Factors arguing for inclusion of ChT are (continued):

- High 21 gene RS (e.g. >25)? Yes No A
- 70 gene High-Risk? Yes No A
- Any positive node? Yes No A
- > 3 positive nodes? Yes No A
- Lymphovascular invasion? Yes No A
- Young age (e.g. < 35 yr)? Yes No A

Chemotherapy
Luminal A

- Is Luminal A phenotype less *responsive* to chemotherapy?
  Yes No A
- Is chemotherapy less *useful* if added to endocrine therapy for pts. with Luminal A phenotype?
  Yes No A
- Is less intensive chemotherapy such as AC4 or CMF6 or TC4 adequate if chemotherapy is considered in Luminal A disease?
  Yes No A
- Should chemotherapy be added for high risk (based on tumour volume)?
  Yes No A

Chemotherapy
Luminal B (HER2 negative)

- Is Luminal B subtype by itself sufficient to prescribe chemotherapy?
  Yes No A
- Is Ki-67 useful in defining Luminal B subtype?
  Yes No A
- If Ki-67 is used, which threshold should be used for defining Luminal B subtype:
  - >= 14%? Yes No A
  - >= 20%? Yes No A
  - >= 25%? Yes No A
  - >= 30%? Yes No A

Chemotherapy

Luminal B (HER2 negative)

- If given, the ChT regimen should contain anthracyclines rather than CMF?

  Yes No A

- Should the regimen contain taxanes?

  Yes No A

- Should chemotherapy extend for at least 6 courses?

  Yes No A

- Should dose-dense ChT be preferred when chemotherapy is indicated?

  Yes No A

Chemotherapy

HER2-positive

- Is there a chemotherapy regimen known to be preferred for HER2-positive phenotype?

  Yes No A

- Need the chemotherapy regimen for HER2-positive disease contain anthracyclines?

  Yes No A

- Need the chemotherapy regimen for HER2-positive disease contain taxanes?

  Yes No A

Chemotherapy

«Basal-Like»

- Should the ChT regimen for «basal-like» (TNBC ductal) phenotype contain anthracyclines and taxanes?
  Yes No A
- Should the ChT regimen for «basal-like» phenotype stress alkylating agents (not merely AC)?
  Yes No A
- Should the ChT regimen for «basal-like» phenotype contain Platinum?
  Yes No A
- Should dose-dense ChT requiring growth factor support be preferred?
  Yes No A

Chemotherapy

Preferences for Regimen

- Are there reasons other than tumor characteristics to prefer specific chemotherapy regimens?
  Yes No A
  - Women desiring fertility preservation?
    Yes No A
  - Avoiding alopecia? Yes No A
  - Co-morbidities? Yes No A
  - Age of patient? Yes No A
  - Intrinsic subtype? Yes No A
  - BRCA carriers? Yes No A
  - Others, specify? Yes No A

Anti-HER2 Therapies

Anti-HER2 Therapy

- Minimum T size (invasive diameter) requiring trastuzumab :
  Vote for 10 mm 5 mm any
- Trastuzumab if given should be concurrent with taxane
  Yes No A
- Trastuzumab if given may be concurrent with anthra.
  Yes No A
- Trastuzumab (+/- endocrine therapy) if ChT contra-indicated?
  - ER positive Yes No A
  - ER negative Yes No A
- Preferred duration of trastuzumab if given:
  Vote for < 1 yr 1 yr > 1 yr

Neo-Adjuvant Systemic Therapies

Neo-Adjuvant Systemic Therapy
Chemotherapy

- Should the only aim of neoadjuvant chemotherapy be to facilitate subsequent local therapies?
  Yes No A
- After pCR to neoadjuvant chemotherapy, subsequent adjuvant chemotherapy:
  - Should be given? Yes No A
  - If so, should include ~~the same~~ agents?
    Yes No A
- After failure to achieve pCR with neoadjuvant chemotherapy, subsequent adjuvant chemotherapy:
  - Should be given? Yes No A
  - If so, should include different agents?
    Yes No A

Neo-Adjuvant Systemic Therapy
HER2-Positive Disease

- Should neoadjuvant regimens for HER2-positive disease contain anti-HER2 drug(s)?

  Yes No A

- Should dual HER2-targeting be recommended in the preoperative setting for HER2-positive disease?

  Yes No A

Neo-Adjuvant Systemic Therapy
Endocrine Therapy

- Is neoadjuvant endocrine therapy alone a reasonable option for postmenopausal patients with *highly endocrine-responsive* disease (e.g. strongly positive receptors, low proliferation)?

  Yes No A

  - If yes, for which duration (choose one)?
  - 3-4 months Yes
  - 4-8 months Yes
  - Maximal response Yes

Bisphosphonates

Bisphosphonates

Is zoledronic acid, given every 6 months during adjuvant endocrine therapy, indicated to improve DFS?

Yes No A

- In premenopausal patients receiving LHRH plus TAM?
  Yes No A
- In premenopausal patients not receiving LHRH?
  Yes No A
- In postmenopausal patients?
  Yes No A
- Should adjuvant denosumab substitute for zoledronic acid?
  Yes No A

Follow up

Follow-up After Early Breast Cancer

- Should all patients have regular follow-up with their surgeon/oncologist after completing their treatment? (excluding long-term endocrine therapy).

  Yes No A

- Is regular follow-up supervised by a nurse specialist in person or by telephone an acceptable follow-up option?

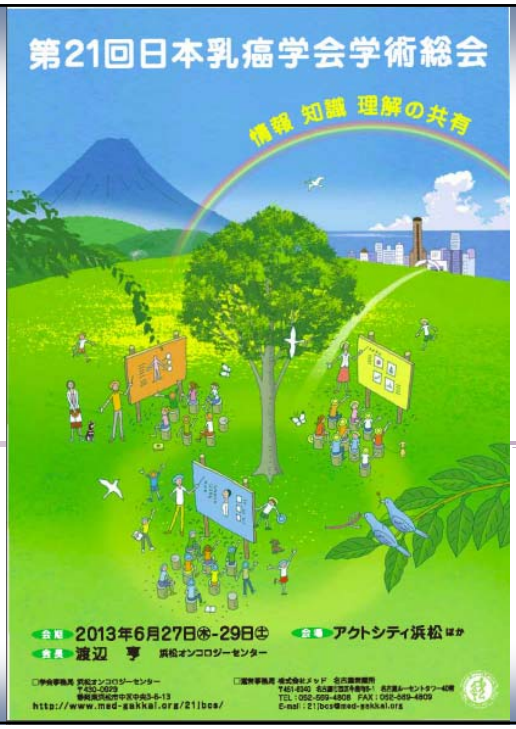
  Yes No A

- Should patients have any form of routine imaging apart from mammography as part of their follow-up?

  Yes No A

君たちにつたえたいこと

- サイエンス、エビデンスを尊重する心をもってほしい
- 日々の診療に埋没せず研究にとりくんでほしい
- 若い時代の貴重な時間を切り売りしないほうがよい
- 寝食を忘れて研究に打ち込んでほしい
- 親はなくとも子は育つ　子供の行事は重視しない
- 時代についていくのではなく時代をリードしてほしい
- 科学的、倫理的な乳がん診療を実践してほしい
- ワークーライフースタディ　バランスを意識してほしい



浜松でお待ちしております。

ホテルはもう予約しましたか？