Achieving the potential of a rapid learning system for cancer

*Patient Care: Moving from current usual care to state-of-the-art and beyond*

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October 6, 2009
Melanoma: Adjuvant treatment planning - today

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The case of Sarah S

- 37 year-old nurse, red haired, Irish
- Tumor characteristics:
  - 3mm ulcerated primary on posterior right arm
  - Single positive sentinel lymph node
  - 0/10 nodes positive on axillary dissection
- Stage IIIB melanoma
  - 47% risk of death at 5 years
  - Standard regimen: 1 month high-dose interferon, 11 months moderate dose; lowers risk of relapse ~10% with unclear impact on survival
  - Associated symptoms: fatigue, mood disturbance, autoimmune dysfunction
- Patient concerns:
  - Family history: Mother died from melanoma
  - Infertility
Adjuvant interferon for Sarah S?
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Observation vs Clinical Trial vs Interferon
### Adjuvant interferon for Sarah S?

<table>
<thead>
<tr>
<th>CLINICAL/PATHELOGIC STAGE</th>
<th>WORKUP</th>
<th>PRIMARY TREATMENT</th>
<th>ADJUVANT TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage III (Sentinel node positive)</td>
<td>Consider baseline imaging for staging and to evaluate specific signs or symptoms (category 2B) (Chest x-ray, CT ± PET, MRI)</td>
<td>Lymph node dissection(^j) or Clinical trial(^k)</td>
<td>Observation or Clinical trial or Interferon alfa(^l) (category 2B)</td>
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</tbody>
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\(^i\) FN has been associated with improved DFS, however, its impact on overall survival is unclear.
Relapse free and overall survival with high dose adjuvant interferon

Fig 2. Relapse-free survival of eligible patients (A) and estimated hazard of relapse over time for eligible patients participating in E1684 (B). OBS, observation.

Fig 3. Overall survival of eligible patients (A) and estimated hazard of death over time for eligible patients participating in E1684 (B).

Impact of interferon on quality of life

Fig 3. Primary health-related quality-of-life end point. Quality of Life Questionnaire (QLQ) -C30 scores for global health status and quality of life, measured by mean score plus 99% CI. PEG-INTRON, pegylated interferon alfa-2b.

Can we shorten the treatment period?

Pectasides et al, JCO 2009 27: 939-44.
The case of Sarah S

- Can generally predict Sarah’s risk of death but cannot refine and personalize these estimates using data from recently treated patients.
- Cannot determine if the right adjuvant management plan – for Sarah.
- Cannot tell Sarah the risk of infertility after treatment.
- Cannot guide Sarah on the direct impact on her personal quality of life, nor the influence of worries about her mother’s death.
- Sarah’s clinical case will not contribute to the care of people in the future unless she is enrolled in a specific clinical trial.
RLHC allows Sarah to benefit from personalized medicine.

- 5 months interferon (1 month high-dose, 4 months moderate-dose) optimizes survival.
- With a <6-month regimen, risk of infertility in a 37yo woman at 5 years is 20%.
- If she gets pregnant, risk of secondary melanoma primaries is 40%.

Data can be used to inform discussion, support clinical decisions, promote new discovery and tailor her care while managing her symptoms/experiences.
Breast Cancer and the Learning Health Care System

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Los Angeles, CA
Adjuvant Therapy Decision-Making

55 y.o. woman with a 1.3 cm hormone receptor positive breast cancer
- Lumpectomy and axillary dissection
- Intermediate grade tumor
- Node negative
- Hormone receptor positive
- Her2/neu negative
- “Doctor, do I need to take chemotherapy?”
Breast Cancer Prognostic Variables

- Tumor size
- Nodal status
- Tumor Grade
- Hormone receptor status
- Her-2-neu status

Well-defined disease outcomes based on a large body of clinical trial evidence!
Use of a treatment decision aid.
Tumor specific prediction is possible

A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer

Soonmyung Paik, M.D., Steven Shak, M.D., Gong Tang, Ph.D., Chungyeul Kim, M.D., Joffre Baker, Ph.D., Maureen Cronin, Ph.D., Frederick L. Baehner, M.D., Michael G. Walker, Ph.D., Drew Watson, Ph.D., Taesung Park, Ph.D., William Hiller, H.T., Edwin R. Fisher, M.D., D. Lawrence Wickerham, M.D., John Bryant, Ph.D., and Norman Wolmark, M.D.

Risk score predicts likelihood of recurrence without chemotherapy.
This patient has her tumor tested and has a recurrence score of 10.
Chemotherapy adds only 2.9% absolute benefit!
A decision is made…

- The patient decides to have chemotherapy even though recurrence score was low.
- She is offered data on comparative efficacy of several adjuvant regimens, and a treatment plan is made.
- Supportive care with anti-emetic therapy is provided using ASCO guidelines to direct therapy.
- Adjuvant endocrine therapy is planned; information from clinical trials comparing tamoxifen to an aromatase inhibitor, with detailed information about treatment outcomes and side effect profiles.
Implications for Decision-making and Management

Opportunities

- Strong evidence base (i.e. Oxford Overview meta-analyses, ASCO & NCCN Guidelines)
- Patient tools to assist informed decision-making
- Tumor based prognostic assessment

Challenges

- Each patient presents with her own complex needs and stage in life/development, and responds accordingly
In RLHC

- Physician uses electronic systems to access linked primary data.
- Physician compares risks/benefits of interferon regimens in context of a patient’s personal characteristics.
- Physician provides tailored guidance, discusses, develops personalized care plan with the patient.
- Symptoms are routinely monitored; patient reported data are used to iteratively refine care.
- Genetics/genomics, imaging, health resource utilization, etc. information are increasingly incorporated as they become available.
- Data from clinical care/response enters personal EHR; it contributes to an ever-growing linked data system available to other providers.
- For subsequent similar patients, providers can query and learn from recent patient-level data that is continuously refined based upon real outcomes.
RLHC: a paradigm that integrates clinical and research spheres

- **Patient level**: PROs, simultaneous clinical and research participation
- **Provider level**: real-time data availability, rapid learning clinics, latest evidence-based care
- **Institution level**: coordination of multi-disciplinary research, networked collaboration
- **Health system level**: linking of clinical and administrative data, continuous QA/QI
- **National level**: RLHC, large-scale shared data repositories and resources (e.g., caBIG), expedited evidence review system