MAGIC survey results

MAGIC data presented at EBCC and IMPAKT
2014
MAGIC committee members

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Introduction

- Treatment recommendations for HR(+), HER2(-) breast cancer patients depend on many factors (eg, tumor size and age)
- Only some patients benefit from adjuvant chemotherapy\(^1\)
- Multigene assays provide prognostic and predictive information beyond traditional parameters, helping to make more-informed treatment decisions
- Treatment decisions and the usage of multigene assays varies per country
- The specific differences and their drivers were evaluated in the MAGIC survey

HR, hormone receptor; HER, human epidermal growth factor
\(^1\)Early Breast Cancer Triallist’Collaborative Group (EBCTG), et al. *Lancet* 2012:379;432-444
Objectives

The MAGIC survey specifically aimed to:

- Identify the criteria clinicians use to determine the need for adjuvant chemotherapy in HR(+) HER2(-) breast cancer
- Study the probability of specific treatment recommendations for simulated breast cancer patients
- Assess for which patient profiles more information is required for treatment decision-making
- Evaluate multigene assay usage and reasons for non-use

HR, hormone receptor; HER, human epidermal growth factor
Methods

The online MAGIC survey (Aug 2013 – Jan 2014) evaluated:
- Respondent characteristics
- General practice patterns
- Criteria considered for treatment decisions
- Simulated treatment recommendations for breast cancer profiles
- Multigene assays usage

Breast cancer clinicians eligible to complete the survey:
- ≥5 years of experience in breast cancer treatment
- Working in multidisciplinary teams
- Treating at least 20 new patients per year

Data analysis by descriptive statistics and a conjoint analysis
SURVEY PARTICIPANTS
Respondents

• Overall, 879 clinicians and 32 pathologists from 52 countries completed the MAGIC survey

• 72% of respondents had >10 years of experience in breast cancer

• 55% of the clinicians indicated to always follow breast cancer treatment guidelines and 43% often followed these guidelines

• St. Gallen (71%), NCCN (54%), ASCO (43%), and ESMO (41%) guidelines were the guidelines that were used most often*

• To facilitate treatment decisions, clinicians most often used Adjuvant! Online (72%), Nottingham Prognostic Index (22%), and PREDICT (12%)*

*Data for guidelines and tools/nomograms is only shown for practicing clinicians (n=879) and multiple answers were allowed
CRITERIA CONSIDERED FOR TREATMENT RECOMMENDATIONS
Conjoint analysis of treatment recommendations

• Methodology of the conjoint analysis
  – By randomly combining patient characteristics, a total of 896 random breast cancer patient profiles were created
  – Each respondent gave treatment recommendations for 24 random patient profiles (chemotherapy, endocrine treatment alone, or a request for more information)

• Rational of the conjoint analysis
  – The respondents’ decisions gave insight into their preferences and clinical criteria they consider when making treatment recommendations
  – Using this information a simulation model could be created to predict treatment recommendations for the 896 patient profiles

For the conjoint analysis only data of the practicing clinicians (n=877) was used
Criteria considered for adjuvant chemotherapy recommendation

- **Age, years**
  - >70
  - 51 - 70
  - 35 - 50
  - <35

- **Grade**
  - Grade 1
  - Grade 2
  - Grade 3

- **Tumor size, cm**
  - <1.0
  - 1.0 - 2.0
  - 2.1 - 3.0
  - 3.1 - 5.0

- **Node status**
  - N0
  - N1

- **Ki67 positivity**
  - < 14%
  - 14% - 20%
  - >20%

- **ER expression**
  - High
  - Low

- **PR expression**
  - High
  - Low

**Index of importance**

ER, estrogen receptor; PR, progesterone receptor
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown
Criteria considered for endocrine treatment alone recommendation

Index of importance

ER, estrogen receptor; PR, progesterone receptor
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown
Criteria considered when requesting more information

Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown.
Increasing age is associated with lower likelihood of chemotherapy recommendations

| Patient profile: 1-2 cm grade 2 tumor, high ER, low PR, 14%-20% Ki67 expression, N0 |
|-------------------------------------------------|----------------|----------------|----------------|----------------|
| Probability for treatment recommendation        | <35 year old patient | 35-50 year old patient | 51-70 year old patient | >70 year old patient |
| Chemotherapy                                    | 69%             | 42%             | 24%             | 5%              |
| Endocrine treatment alone                       | 12%             | 31%             | 48%             | 72%             |
| More information                                | 19%             | 27%             | 28%             | 23%             |

- Patient age affects simulated probabilities for different treatment recommendations
- Older patients have a lower probability to be recommended chemotherapy (and vice versa)

ER, estrogen receptor; PR, progesterone receptor; N0, node negative
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown
Increasing tumor grade is associated with higher chemotherapy recommendation rates.

<table>
<thead>
<tr>
<th>Probability for treatment recommendation</th>
<th>Patient with grade 1 tumor</th>
<th>Patient with grade 2 tumor</th>
<th>Patient with grade 3 tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>22%</td>
<td>42%</td>
<td>75%</td>
</tr>
<tr>
<td>Endocrine treatment alone</td>
<td>53%</td>
<td>31%</td>
<td>8%</td>
</tr>
<tr>
<td>More information</td>
<td>25%</td>
<td>27%</td>
<td>17%</td>
</tr>
</tbody>
</table>

- Tumor grade affects simulated probabilities for different treatment recommendations.
- Patient with tumors with a higher grade have a higher probability to be recommended chemotherapy.

ER, estrogen receptor; PR, progesterone receptor; N0, node negative
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown.
Low ER expression is associated with increased likelihood of chemotherapy recommendation

Patient profile: 35-50 year old, 1-2 cm grade 2 tumor, low PR, 14%-20% Ki67 expression, NO

<table>
<thead>
<tr>
<th>Probability for treatment recommendation</th>
<th>Patient with tumor with high ER expression</th>
<th>Patient with tumor with low ER expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>42%</td>
<td>72%</td>
</tr>
<tr>
<td>Endocrine treatment alone</td>
<td>31%</td>
<td>6%</td>
</tr>
<tr>
<td>More information</td>
<td>27%</td>
<td>22%</td>
</tr>
</tbody>
</table>

- Tumor ER expression affects simulated probabilities for different treatment recommendations
- Patient with tumors with a low ER expression have a higher probability to be recommended chemotherapy

ER, estrogen receptor; PR, progesterone receptor; N0, node negative
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown
Nodal involvement is associated with increased likelihood of chemotherapy recommendation.

Patient profile: 35-50 year old, 1-2 cm grade 2 tumor, high ER, low PR, 14%-20% Ki67 expression

<table>
<thead>
<tr>
<th>Probability for treatment recommendation</th>
<th>N0 patient</th>
<th>N1-3 patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>42%</td>
<td>77%</td>
</tr>
<tr>
<td>Endocrine treatment alone</td>
<td>31%</td>
<td>6%</td>
</tr>
<tr>
<td>More information</td>
<td>27%</td>
<td>17%</td>
</tr>
</tbody>
</table>

- The nodal status of the patient affects simulated probabilities for different treatment recommendations.
- Node-positive patients have a higher probability to be recommended chemotherapy.

ER, estrogen receptor; PR, progesterone receptor; N0, node negative; N1-3, one to three positive nodes
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown.
Criteria considered for treatment recommendations

• Age is considered the most important patient characteristic for each treatment recommendation

• Small changes in patient characteristics can have a large influence on treatment recommendations

• Patient profiles associated with a request for more information tend to have an intermediate/higher age, intermediate/smaller tumor of grade 1 or 2, and low estrogen receptor expression, and intermediate Ki67 expression (14–20%)
PROBABILITY OF TREATMENT RECOMMENDATIONS (PER COUNTRY)
Proportion of cases with >50% probability of a chemotherapy recommendation

Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown (conjoint analysis)
Proportion of cases with >50% probability of recommending an endocrine treatment alone.

Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown (conjoint analysis).
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown (conjoint analysis)
Effect of patient characteristics and country on treatment recommendations

Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown for patients with the following characteristics:
- 51-70 year old
- 1-2 cm grade 2 tumor
- High ER, low PR
- 14%-20% Ki67 expression
- N0

<table>
<thead>
<tr>
<th>Probability for treatment recommendation</th>
<th>All</th>
<th>MX</th>
<th>GR</th>
<th>ES</th>
<th>BE</th>
<th>RU</th>
<th>FR</th>
<th>AR</th>
<th>IT</th>
<th>SE</th>
<th>DE</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>24%</td>
<td>34%</td>
<td>31%</td>
<td>30%</td>
<td>28%</td>
<td>28%</td>
<td>27%</td>
<td>24%</td>
<td>20%</td>
<td>20%</td>
<td>19%</td>
<td>16%</td>
</tr>
<tr>
<td>Endocrine treatment alone</td>
<td>48%</td>
<td>34%</td>
<td>27%</td>
<td>35%</td>
<td>48%</td>
<td>59%</td>
<td>47%</td>
<td>39%</td>
<td>62%</td>
<td>69%</td>
<td>43%</td>
<td>61%</td>
</tr>
<tr>
<td>More information</td>
<td>28%</td>
<td>32%</td>
<td>42%</td>
<td>35%</td>
<td>24%</td>
<td>13%</td>
<td>26%</td>
<td>37%</td>
<td>18%</td>
<td>11%</td>
<td>38%</td>
<td>23%</td>
</tr>
</tbody>
</table>

- There is a large variation between countries in the probability for treatment recommendations for one given patient profile

ER, estrogen receptor; PR, progesterone receptor; N0, node negative
Effect of patient characteristics and country on treatment recommendations

Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown

**Patient profile:** 51-70 year old, 1-2 cm grade 3 tumor, high ER, low PR, 14%-20% Ki67 expression, N0

<table>
<thead>
<tr>
<th>Probability for treatment recommendation</th>
<th>All</th>
<th>SE</th>
<th>ES</th>
<th>BE</th>
<th>FR</th>
<th>GR</th>
<th>MX</th>
<th>DE</th>
<th>IT</th>
<th>RU</th>
<th>UK</th>
<th>AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>60%</td>
<td>71%</td>
<td>68%</td>
<td>67%</td>
<td>66%</td>
<td>63%</td>
<td>60%</td>
<td>60%</td>
<td>57%</td>
<td>56%</td>
<td>56%</td>
<td>49%</td>
</tr>
<tr>
<td>Endocrine treatment alone</td>
<td>19%</td>
<td>21%</td>
<td>9%</td>
<td>16%</td>
<td>13%</td>
<td>8%</td>
<td>12%</td>
<td>15%</td>
<td>29%</td>
<td>31%</td>
<td>25%</td>
<td>17%</td>
</tr>
<tr>
<td>More information</td>
<td>21%</td>
<td>8%</td>
<td>23%</td>
<td>17%</td>
<td>21%</td>
<td>29%</td>
<td>28%</td>
<td>25%</td>
<td>14%</td>
<td>13%</td>
<td>19%</td>
<td>34%</td>
</tr>
</tbody>
</table>

- Changing the tumor grade from grade 2 to grade 3 increases the likelihood of chemotherapy recommendation, but the extent of this increase depends on the country of residence

ER, estrogen receptor; PR, progesterone receptor; N0, node negative

Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown
Effect of patient characteristics and country on treatment recommendations

Patient profile: 51-70 year old, 1-2 cm grade 2 tumor, high ER, low PR, 14%-20% Ki67 expression, N1-3

<table>
<thead>
<tr>
<th>Probability for treatment recommendation</th>
<th>All</th>
<th>SE</th>
<th>ES</th>
<th>FR</th>
<th>BE</th>
<th>GR</th>
<th>MX</th>
<th>RU</th>
<th>UK</th>
<th>IT</th>
<th>AR</th>
<th>DE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>66%</td>
<td>78%</td>
<td>72%</td>
<td>71%</td>
<td>70%</td>
<td>69%</td>
<td>69%</td>
<td>67%</td>
<td>65%</td>
<td>60%</td>
<td>55%</td>
<td>54%</td>
</tr>
<tr>
<td>Endocrine treatment alone</td>
<td>13%</td>
<td>13%</td>
<td>7%</td>
<td>9%</td>
<td>11%</td>
<td>5%</td>
<td>8%</td>
<td>23%</td>
<td>14%</td>
<td>26%</td>
<td>8%</td>
<td>13%</td>
</tr>
<tr>
<td>More information</td>
<td>21%</td>
<td>9%</td>
<td>21%</td>
<td>20%</td>
<td>19%</td>
<td>26%</td>
<td>23%</td>
<td>10%</td>
<td>21%</td>
<td>14%</td>
<td>37%</td>
<td>33%</td>
</tr>
</tbody>
</table>

- For this patient profile, changing the nodal status of a patient from N0 (slide 22) to N1-3 increases the likelihood of a chemotherapy recommendation more than changing the tumor grade from grade 2 to 3
- The extent of this increase again depends on the country of residence

ER, estrogen receptor; PR, progesterone receptor; N0, no positive nodes; N1-3, one to three positive nodes

Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown
Effect of patient characteristics and country on treatment recommendations

Patient profile: 51-70 year old, 1-2 cm grade 3 tumor, high ER, low PR, 14%-20% Ki67 expression, N1-3

<table>
<thead>
<tr>
<th>Probability for treatment recommendation</th>
<th>All</th>
<th>SE</th>
<th>ES</th>
<th>FR</th>
<th>BE</th>
<th>RU</th>
<th>UK</th>
<th>IT</th>
<th>GR</th>
<th>MX</th>
<th>DE</th>
<th>AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>85%</td>
<td>94%</td>
<td>89%</td>
<td>88%</td>
<td>87%</td>
<td>86%</td>
<td>86%</td>
<td>85%</td>
<td>83%</td>
<td>82%</td>
<td>81%</td>
<td>70%</td>
</tr>
<tr>
<td>Endocrine treatment alone</td>
<td>3%</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
<td>6%</td>
<td>2%</td>
<td>6%</td>
<td>1%</td>
<td>2%</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>More information</td>
<td>12%</td>
<td>5%</td>
<td>10%</td>
<td>11%</td>
<td>11%</td>
<td>8%</td>
<td>12%</td>
<td>9%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>28%</td>
</tr>
</tbody>
</table>

- Comparing similar patient profiles demonstrate that both patient characteristics and the clinician’s country of residence strongly affect the simulated probabilities for certain treatment recommendations.

ER, estrogen receptor; PR, progesterone receptor; N1-3, one to three positive nodes
Simulated data based on treatment recommendations of practicing clinicians (n=877) is shown.
MULTIGENE ASSAY USAGE (GENERAL)
Multigene assay usage

Only data for practicing clinicians is shown (n=879)
Multigene assay usage stratified by users of tools/nomograms

Only data for practicing clinicians is shown (n=879)
Multigene assay usage stratified by Ki67% consideration

Only data for practicing clinicians is shown (n=879)
Multigene assay usage

- Although almost all clinicians would like to use multigene assays in a subset of HR(+) HER2(-) breast cancers, the usage of multigene assays varies substantially between countries.

- Clinicians that do not use tools/nomograms tend to use multigene assays less often.

- Clinicians that do not consider Ki67 expression for their treatment recommendations tend to use multigene assays more often (unless they have no access to Ki67% testing).

HR, hormone receptor; HER, human epidermal growth factor.
MULTIGENE ASSAY USAGE
(PER COUNTRY)
Used multigene assays per country

Overall 
Argentina 
Belgium 
France 
Germany 

Greece 
Hungary 
Italy 
Mexico 
The Netherlands 

Russia 
Spain 
Sweden 
Switzerland 
UK 

The country specific data can be obtained by selecting the country of interest
Of 879 practicing clinicians, 55% (n=485) used multigene assays and answers for this group are shown (multiple answers were allowed). “Other” answers included genomic grade index, Stratifyer, IHC4, and MammaGene.
Multigene assay usage

- The usage of multigene assays strongly varies between countries (55% of all respondents use them).

- Multigene assays are most often used in Greece (91%), Germany (89%), and The Netherlands (89%).

- Among multigene assay users, Oncotype DX® Breast Cancer Assay (78%) and MammaPrint® (34%) are the most frequently used assays in the majority of the countries.
REASONS FOR NOT USING MULTIGENE ASSAYS (PER COUNTRY)
Reasons for not using multigene assays per country

Overall, Argentina, Belgium, France, Germany, Greece, Hungary, Italy, Mexico, The Netherlands, Russia, Spain, Sweden, Switzerland, UK

The country specific data can be obtained by selecting the country of interest.
Of 879 practicing clinicians, 394 (45%) did not use multigene assays of which 389 answered this question. Results are shown for that group (multiple answers were allowed).
Multigene assay non-usage

• Of those that do not use multigene assays, 87% would like to use them

• The reasons for not using multigene assays varies between countries

• The main reported barriers to multigene assay usage are a lack of reimbursement, price, and a lack of availability
SUMMARY AND CONCLUSIONS
Treatment recommendations

- Treatment recommendations for early stage HR(+), HER2(-) breast cancer patient varies substantially between countries.

- Age is considered to be the most important patient characteristic for the recommendation of chemo-endocrine/endocrine therapy.

- Treatment recommendations are more homogeneous for patients with a combination of only low-risk or only high-risk characteristics.

- The highest variability in treatment recommendations is seen for patients with intermediate risk parameters.

HR, hormone receptor; HER, human epidermal growth factor.
Multigene assay usage

• Due to the high heterogeneity in treatment recommendations there is a need for broadly available tools, such as multigene assays, to help make more-informed treatment decisions

• The majority of respondents use multigene assays or would like to use them

• Oncotype DX® Breast Cancer Assay, followed by MammaPrint®, is the most often used multigene assay

• The usage of multigene assays varies between countries, mainly related to a lack of reimbursement, the price, and a lack of availability
BACK-UP SLIDES
Usage of multigene assays by country

Only data for practicing clinicians is shown (n=879), multiple answers were allowed.
Reasons for not using multigene assays

Only data for practicing clinicians is shown (n=879), multiple answers were allowed.