热门文章

赫赛汀在早.. [12.13]
21基因表达.. [10.5]
注射用紫杉.. [11.5]
紫杉醇一白.. [12.18]
绝经后受体.. [3.11]
HER-2阳性.. [11.5]
赫赛汀在H.. [10.5]
赫赛汀用在.. [12.18]
有高危因素.. [12.14]
Trastuzum.. [11.5]
紫杉醇每周.. [11.9]
早期乳腺癌.. [8.10]
乳腺癌疗效.. [8.10]
阿霉素联合.. [3.11]

推荐文章

赫赛汀在H.. 刘冬耕 史艳侠
21基因表达.. 刘冬耕 史艳侠

AACR:PIK3CA基因突变情况可能影响HER2阳性乳癌的治疗策略

作者：[中国肿瘤化疗] 来源：[本站] 浏览：[] 评论：[]

AACR:PIK3CA基因突变情况可能影响HER2阳性乳癌的治疗策略

中国肿瘤化疗 来源：MedScape 发布日期：2013-4-15

PIK3CA基因突变的乳癌患者会对包括trastuzumab（Herceptin）和lapatinib (Tykerb)在内的常规HER2靶向治疗耐药。但根据在AACR上报道的对EMILIA研究的亚分析数据，FDA2月批准的乳癌新药trastuzumab emtansine (Kadcyla，TDM1)治疗乳癌的疗效并不受PIK3CA基因突变情况的影响。

研究者认为HER2阳性乳癌并不是一种单一的疾病，应该对患者进行细分。

在既往的报道中，接受T-DM1治疗患者的PFS与OS都优于拉帕替尼加卡培他滨治疗者（PFS:9.6月 vs 6.4月 ；OS:30.9月 vs 25.1月）。而亚分析研究显示，无论患者的PIK3CA基因是否突变，T-DM1的疗效是一样的；而接受拉帕替尼加卡培他滨治疗的患者中，PIK3CA基因突变患者的疗效显著差于无突变患者。

这些研究数据为根据PIK3CA基因突变情况选择不同HER2治疗策略的理论提供了更多的证据。不过，目前尚不能把该理论应用于临床实践，因为已有的相关研究都是回顾性分析得到的数据，还需前瞻性研究验证。不过，研究者认为应该在临床实践中对HER2阳性乳癌患者例行PIK3CA基因突变情况的检测。

Mutation Status May Guide Treatment for HER2 Breast Cancer

Nick Mulcahy Apr 10, 2013

WASHINGTON, DC — The effectiveness of trastuzumab emtansine (Kadcyla, Genentech), which was recently approved for the second-line treatment of metastatic HER2-positive breast cancer, is apparently not diminished by tumor mutations in the PIK3CA gene.

This is good news for clinicians because PIK3CA mutations can lead to resistance to conventional HER2-directed therapies, such as trastuzumab (Herceptin, Genentech) and lapatinib (Tykerb, GlaxoSmithKline), said José Baselga, MD, PhD, from the Memorial Sloan-Kettering Cancer Center in New York City.

Dr. Baselga spoke at a press conference here at the American Association for Cancer Research 104th Annual Meeting.

He explained that trastuzumab emtansine, also known as T-DM1, is different from other drugs for HER2-positive disease because it has the mechanisms of action of trastuzumab, a targeted therapy, but also delivers a "very potent" chemotherapy, emtansine, directly to tumors.

Dr. Baselga presented new data from the EMILIA study, which was the basis for the approval of T-DM1 in metastatic disease.

Dr. Baselga reported that, consistent with previous findings, patients treated with T-DM1 had significantly better progression-free survival (9.6 vs 6.4 months) and overall survival (30.9 vs 25.1 months) than patients treated with lapatinib and capecitabine.

In addition, he presented a new subanalysis that examined the relation between treatment efficacy and a number of biomarkers, including the PIK3CA mutation.

Our findings are an important step toward identifying the best therapy for individual patients.

"Our findings [on biomarkers] are an important step toward identifying the best therapy for individual patients with HER2-positive breast cancer," said Dr. Baselga in a press statement. "HER2-positive breast cancer is not a uniform disease; each patient is different."

The investigators found that patients treated with T-DM1 had similar outcomes, regardless of their PIK3CA status, but that patients treated with lapatinib and capecitabine did worse if they had the mutation.

These data provide further evidence that mutations in the PIK3CA gene might be important in selecting the appropriate HER2 therapy.

"Our results are not practice changing at this point" because they are retrospective and need confirmation, said Dr. Baselga. "But I think we should start sequencing and checking for the presence of PIK3CA mutations," he added.

Another expert, who is not involved with the study, had similar thoughts and suggested that the testing should be performed for all women with HER2-positive breast cancer.

If you have it, then you may be less sensitive to trastuzumab and lapatinib.

"In the future, we should test for the PIK3CA mutation because, if you have it, then you may be less sensitive to trastuzumab and lapatinib," said Giuseppe Giaconne, MD, PhD, from the Georgetown Lombardi Comprehensive Cancer Center in Washington, DC, and the National Cancer Institute. When he spoke with Medscape Medical News at the meeting, he emphasized that the findings need to be repeated in a prospective trial.

If testing becomes standard, then treatment decisions for patients with HER2-positive disease would be based, in part, on PIK3CA status, he explained.

This information should pave the way for earlier and wider use of T-DM1 in HER2-positive breast cancer patients, Dr. Giaconne said.

There are now 4 therapies that target HER2-positive metastatic breast cancer, and T-DM1 is the most expensive. According to media reports, trastuzumab costs around $4500 per month, pertuzumab costs around $6000 per month, and T-DM1 costs around $9800 per month. Some clinicians are very concerned about the escalating cost of these therapies.

Amount of HER2 Also Matters

Dr. Baselga and colleagues reviewed data from the 991-patient EMILIA trial to retrospectively look at specific biomarkers, including the PIK3CA mutation, and their possible influence on treatment outcomes.

Tumor tissue collected for HER2 testing was also used to assess PIK3CA in a subset of 259 patients — 133 treated with T-DM1 and 126 treated with lapatinib and capecitabine.

In the T-DM1 group, progression-free survival, the primary study outcome, was somewhat better in the 40 patients with PIK3CA mutations than in the 93 patients with wild-type PIK3CA (10.9 vs 9.8 months). Overall survival was comparable between the 2 groups.

In other words, in the T-DM1 group, PIK3CA mutations did not mean worse outcomes.

This was not the case for the patients treated with lapatinib and capecitabine; PIK3CA mutations meant worse progression-free and overall survival in that group.

Specifically, in the lapatinib and capecitabine group, progression-free survival was worse in the 39 patients with PIK3CA mutations than in the 87 patients with wild-type PIK3CA (4.3 vs 6.4 months). Overall survival was also worse in patients with the mutation.

The investigators also assessed the associaiton between tumor levels of HER2, based on the amount of HER2 messenger (m)RNA, and treatment outcome.

Patients with tumor samples expressing greater than the median amount of HER2 mRNA were considered to have high levels of HER2. Those with tumor samples expressing the median amount of HER2 mRNA or less were considered to have low levels of HER2.

For patients treated with T-DM1, overall survival was better for tumors expressing higher levels of HER2 than for tumors expressing lower levels (34.1 vs 26.5 months).

The study was sponsored by Genentech and Roche. Dr. Baselga reports financial relationships with Roche and other pharmaceutical companies. Dr. Giaconne has disclosed no relevant financial relationships.

American Association for Cancer Research (AACR) 104th Annual Meeting: Abstract LB-63. Presented April 8, 2013.

上一篇：已到尽头
下一篇：五分之一以上的乳腺癌患者发生上肢淋巴水肿
【 打印 】【 收藏 】【 评论 】【 推荐 】

评一评

正在读取…

笔名：

评论：

发表评论 重写评论