治療により進行前立腺がんの生存期間が延長する (Abstract 5001)

STAMPEDE：初回治療に化学療法を追加することにより進行ホルモン療法未治療前立腺がん患者の寿命が延長する

STAMPEDE: Adding chemotherapy to initial therapy extends lives of men with advanced, hormone-naïve prostate cancer

Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy（STAMPEDE）トライアルの結果、標準的なホルモン療法にドセタキセルによる化学療法を追加することにより、ホルモン治療歴のない新たに診断された進行前立腺がん患者の生存期間が改善する、と第51回American Society of Clinical Oncology年次集会で発表された。研究者らは、ホルモン療法未治療の患者2,962人をSTAMPEDEの9つの治療群のうち4つ：標準治療（SOC）、SOCとドセタキセルを6サイクル、SOCとゾレドロン酸を2年間、およびSOCとドセタキセルおよびゾレドロン酸の両者に割り付けた。約60%の患者がトライアル参加時に転移を有しており、その他は高リスク、局所進行非転移前立腺がん（リンパ節転移陰性、ステージT3/4、PSA≥40ng/mlまたはGleasonスコア8-10）を有していた。追跡期間中央値42か月後に、948人が死亡した。全生存期間はドセタキセル群においてSOC群よりも平均10か月長く（67対77か月）、相対的改善率は24%であった。転移性疾患患者においては、全生存期間における平均改善率はさらに大であった（43対65か月）。ドセタキセルはまた、全ての患者において再発までの期間を38%延長させた。

Full Text

The UK-led trial Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (STAMPEDE) found that adding docetaxel chemotherapy to standard hormone therapy markedly improves survival for men with newly diagnosed advanced prostate cancer not previously treated with hormone therapy according to researchers at the American Society of Clinical Oncology's 51st Annual Meeting. Men who received docetaxel plus standard therapy lived on average ten months longer than those who received only standard therapy. In contrast, adding zoledronic acid to standard therapy did not affect survival, and adding the combination of zoledronic acid and docetaxel was not more effective than adding just docetaxel.

"We hope our findings will encourage doctors to offer docetaxel to men newly diagnosed with metastatic prostate cancer, if they are healthy enough for chemotherapy. Men with locally advanced, non-metastatic prostate cancer may also consider docetaxel as part of upfront therapy, as it clearly delays relapse," said lead study author Nicholas David James, M.D., Ph.D., Director of the Cancer Research Unit at the University of Warwick in Coventry, United Kingdom and Consultant in Clinical Oncology at Queen Elizabeth Hospital Birmingham. "It's also clear that zoledronic acid does not benefit these patients and should not be offered as an upfront treatment for advanced prostate cancer."

STAMPEDE (Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy), is the largest randomized clinical trial of treatment for men with prostate cancer ever conducted, with more than 6,500 patients enrolled since 2005. The ongoing study has an innovative multi-stage, multi-arm design that can be modified to both assess new therapies and adapt to changes in the standard of care. The standard of care (SOC) in the continuously recruiting control arm changes as treatment patterns change. For example, radiation therapy has been added to the mainstay androgen deprivation therapy for certain patients. As the trial goes on, treatment arms that are found to be ineffective are stopped, and new arms are added to assess the efficacy of emerging treatments, such as novel hormone drugs.

At ASCO's Annual Meeting, researchers reported results on 2,962 hormone-naïve men who were assigned to four of STAMPEDE's nine different treatment arms: SOC, SOC with docetaxel for six cycles, SOC with zoledronic acid for two years, and SOC with both docetaxel and zoledronic acid. The SOC was at least three years of androgen deprivation therapy, with local radiation for suitable patients. About 60% of the patients had metastatic disease when joining the trial and the rest had high-risk, locally advanced non-metastatic prostate cancer (node-negative, stage T3/4, PSA≥40ng/ml or Gleason sum score 8-10).

After a median follow-up of 42 months, 948 men had died. Overall survival was on average ten months longer in the docetaxel arm compared to the SOC arm (67 vs. 77 months) with a relative improvement of 24%. For the subset of patients with metastatic disease, the average improvement in overall survival was even higher, 22 months (from 43 vs. 65 months). Importantly, docetaxel also extended the time to relapse by 38% in all patients.

Two previous, smaller trials have reported results on using docetaxel in the hormone-naïve metastatic setting. These trials showed conflicting results. CHAARTED in the USA reported in the plenary session of ASCO 2014 showed a survival advantage; GETUG-15 in France did not. STAMPEDE goes a long way in clarifying the role of docetaxel in men with newly diagnosed, high-risk prostate cancer. The trial also included a larger and broader patient population than those trials, comprising men with metastatic prostate cancer and 600 men with locally advanced, non-metastatic disease.

According to the authors, the overall findings of this study suggest that men with newly diagnosed metastatic prostate cancer should be offered docetaxel as part of their initial therapy. They suggest that doctors may also discuss the option of adding docetaxel with patients who have advanced, non-metastatic prostate cancer, given the reduction in risk of relapse seen in this study. However, longer follow-up is needed to determine if there is any survival advantage in men with non-metastatic disease.

While docetaxel was associated with some additional toxicity compared to SOC alone, the side effects were manageable, and very few patients discontinued docetaxel due to side effects. Results of a quality of life analysis will be reported at a later time.

The difference in survival was not statistically significant between the SOC and SOC plus zoledronic acid arm. Addition of zoledronic acid to the combination of SOC and docetaxel yielded similar outcomes as SOC with only docetaxel.

"This is the biggest trial of its kind and strongly suggests that adding chemotherapy to standard hormone therapy can extend the lives of men with advanced prostate cancer" comments ASCO President Peter Paul Yu, M.D., FACP, FASCO. "Its innovative design is exciting, and one that we may begin to see in other areas of oncology."

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