Manitoba Prostate Cancer SUPPORT GROUP

Newsletter

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Immunotherapy 'May Help Advanced Prostate Cancer Patients'

CHICAGO — A small proportion of men with advanced prostate cancer for whom other treatments have failed may experience a significant and ongoing benefit with the programmed death ligand 1 (PD-L1) inhibitor pembrolizumab (Keytruda, Merck), say UK researchers who are now working on how to reliably identify those men.

Intriguingly, the immunotherapy, which continued to show a benefit after a year in 11% of the 258 men with metastatic castration-resistant prostate cancer (mCRPC), appeared to have a benefit even in men who did not express PD-L1.

Presenting the new data here at the American Society of Clinical Oncology (ASCO) 2018 Annual Meeting, Professor Johann De Bono, from the Royal Marsden Hospital, London, suggested that genetic biomarkers may point to those who are at risk, although the data were preliminary.

He said: "In a small population of patients with advance prostate cancer, pembrolizumab clearly has some anti-tumour activity, and activity was observed in PD-L1 positive and negative groups."

De Bono added: "Biomarker work is ongoing and we have clearly seen of antitumour activity in mismatch repair defective cancers, in at least one definite BRAC2 mutated cancer, as well as some patients that we still don't fully understand why they responded.

(Continued on page 2)

Medical Advisors

Paul Daeninck M.D.
Medical Oncologist

Darrel Drachenberg M.D. Urologist

Arbind Dubey M.D.
Radiation Oncologist

Thanks!

Next Meeting:

Wednesday, July 18, 2018

Speaker: Dr. David Dawe

Title: "Advances in treating hormone-resistant prostate cancer"

Location: The First Unitarian Universalist Church of Winnipeg, 603 Wellington Crescent

Time: 7 – 9 pm.
(First hour for general discussion; second hour for expert guest speaker)

Free Admission Everyone Welcome
Plenty of free parking

SHARING IS CARING

The Manitoba Prostate Cancer Support Group offers support to prostate cancer patients but does not recommend any particular treatment modalities, medications or physicians ; such decisions should be made in consultation with your doctor.

MPCSG – active since 1992.

Thought of The Day

*When I fill out an application, in the part that says "In an emergency, notify . . . ," I put "**doctor**."*

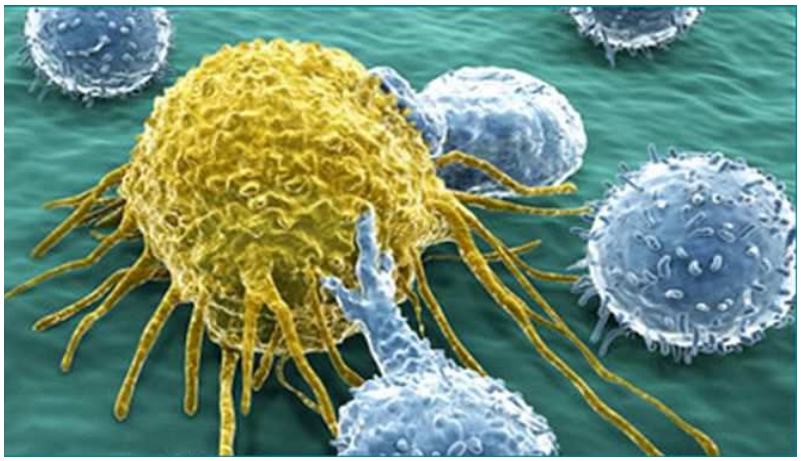
(Continued from page 1)

"Further evaluation of the subset that respond is ongoing, as are combination trials in this population of patients."

'Smarter, Kinder Treatment'

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, whose researchers also took part in the trial, said in a press release: "Immunotherapy has proven to be a smarter, kinder treatment for many types of cancer, but it still only works for a minority of patients.

"The challenges we now face are how to predict in advance who will benefit, and how to make immunotherapy work for more people."



Workman added that, if if gene mutations can be shown to identify the patients who will respond, "it should be possible to provide some men with advanced prostate cancer with an exciting new treatment option."

Latest Research

Although PD-1 and PD-L1 inhibitors have shown activity in numerous cancers, there have been few signs of activity in prostate cancer.

However, two recent studies, including KEYNOTE-028, suggested that pembrolizumab may achieve objective responses in some men with previously treated PD-L1-positive mCRPC.

De Bono told the audience that KEYNOTE-199 was therefore launched to try to confirm this activity and determine which patents might benefit from PD-L1 blockade.

Of the five cohorts included in the study, he focused on three, which included mCRPC patients who had received ≥1 prior targeted endocrine therapy and who had undergone 1–2 prior chemotherapy regimens, including docetaxel (Taxotere, Sanofi-Aventis). All patients also had an ECOG performance status of 0–2.

In cohort one (n=131), all of the men had PD-L1-positive mCPRC, while those in cohort two (n=67) had PD-L1-negative disease. In both groups, the patients had measurable disease as per the Response Evaluation Criteria In Solid Tumours (RECIST) v1.1 criteria.

In cohort three (n=60), the patients had bone metastases but no measurable disease on RECIST v1.1, and had any PD-L1 status.

Patients in all three cohorts were treated with pembrolizumab 200 mg for 35 weeks or until confirmed progressive disease, intolerable toxicity, investigator decision or patient withdrawal.

The patients, who fitted the typical post-chemotherapy patient profile, underwent imaging every 9 weeks for 1 year and then every 12 weeks. The primary endpoint was the objective response rate as per RECIST v1.1 in cohorts one and two.

After a median follow-up of 8.1 months in cohort one, 11% of patients were still being treated at the data cut-off for the study. In cohort two, 9% were still receiving treatment after a median of 7.9 months, while, in cohort three, 12% were still on treatment after 11.8 months of follow-up.

In cohorts one and two, 10% of patients had a change in the sum of the target lesions from baseline of ≥30% with pembrolizumab, while 11% of patients in all three cohorts had a reduction in prostate-specific antigen levels from baseline of ≥50%.

In both cases, the responders to pembrolizumab therapy included those who did not have any measurable PD-L1.

Central review of the best responses indicated that, in cohort one, 2% of patients had a complete response, 4% had a partial response, and 17% had stable disease, with 4% having stable disease for ≥6 months.

In cohort two, 3% of patients had a partial response and 21% had stable disease, which lasted for ≥6 months in 3%. There were no responses to treatments in cohort three on central review.

The researchers calculated that the disease control rate lasting ≥6 months, which included the best response of complete or partial response of stable disease, across all three cohorts was 11%.

"So we have clearly evidence of a small population that is benefiting," said De Bono.

After 12 months, 39% of patients in

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cohort one were still alive, while 38% of cohort two patients were still alive, alongside 61% of cohort three patients, although De Bono emphasised that the non-randomised nature of the trial means that it is "hard to draw conclusions" from the data.

Interestingly, genomic analysis of responders to pembrolizumab suggested that there may be some gene mutations that could be associated with response, such as in the BRCA2 gene.

Indeed, analysis of response by the presence of somatic aberrations in DNA repair genes indicated that patients with BRCA1/2 or ATM gene mutations had a disease control rate of 22%.

De Bono noted that 59% of patients across the trial cohorts had any treatment-related adverse events, and 14% had grade 3–5 adverse events. The most common treatment-related events were fatigue (15%) and diarrhoea (10%), while the immune-mediated events included hyperthyroidism and hypothyroidism.

'Curious'

Study Discussant Dr Douglas McNeel, from the University of Wisconsin School of Medicine and Public Health, Madison, in the US, said following its presentation, that the objective response rates in cohorts one and two are "fairly small, and it's curious that there is no difference between the patients who are PD-L1 positive and PD-L1 negative".

He added: "While I think there's activity there, it's smaller and definitely different from what we've seen with PD-L1 blockade in other diseases."

McNeel agreed with the conclusion that DNA repair defects may be associated with the antitumour activity seen in the study, saying that this "could be important, since the rate of homologous recombination repair mutations is likely higher than microsatellite instability."

He said that the data suggests that this, nevertheless, "may be a premature conclusion but certainly worth more attention".

The study was funded by Merck Sharp & Dohme.

American Society of Clinical Oncology (ASCO) 2018 Annual Meeting. Presented June 4, 2018. Abstract 5007.

Liam Davenport June 07, 2018

https://www.medscape.com/viewarticle/897769

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To us it matters because we want the newsletter to reach the maximum number of prostate cancer patients who want to receive it. This involves having both hardcopy (mailed to you via snail mail) and electronic forms (delivered via the internet) available. Hardcopy is the traditional form, and reaches all those members who do not have access to the internet or who prefer the traditional format for whatever reason. For those who do have internet access the electronic form can be delivered via email message to you or it can be directly accessed by going to our website (manpros.org) and clicking on the "newsletter" tab.

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~ The Board.

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Prostate Cancer Surgery: What You Should Know

Summary
Surgery can cure prostate cancer if the disease hasn't spread outside of the prostate gland. The most common procedure is a radical prostatectomy. It can be done as traditional open surgery or in a minimally invasive approach, including robot-assisted laparoscopic surgery. Regardless of method, the most important factor is choosing a surgeon with extensive expertise to get the best results and reduce the risk of complications.

Prostate cancer is the most common form of cancer in men after skin cancer. Surgery is very effective at controlling or curing the disease.

We spoke with James Eastham, Chief of Memorial Sloan Kettering's Urology Service, about different ways of performing prostate cancer surgery, the side effects that may be involved, and the importance of having an experienced surgeon do the procedure.

When is prostate cancer surgery most effective?
Surgery is a curative treatment for prostate cancer when the disease has not yet spread to organs or tissues outside of the prostate gland. In these instances, the long-term prognosis is excellent.

If the cancer has spread beyond the prostate, we can still achieve good outcomes with radiation therapy or systemic therapy following surgery. This includes chemotherapy, hormone therapy, biologic therapy, or immunotherapy.

Some people whose disease is confined to the prostate choose not to have — or at least to delay — surgery. We monitor them closely, a strategy known as active surveillance. This choice is a joint decision between the doctor and patient. It is best for small tumors that are growing slowly and are considered at low risk of spreading. For each patient, it is a personal decision.

What are the different types of prostate cancer surgery?
The most common one is called a radical prostatectomy. In this procedure, the entire prostate gland is removed, along with some of the surrounding tissue. In some cases, nearby lymph nodes are removed as well. There are several surgical approaches for this, including traditional open surgery. We can also use minimally invasive procedures, such as laparoscopic surgery and robot-assisted laparoscopic surgery.

Urology Service Chief James Eastham says men should seek out a highly experienced surgeon with whom they feel comfortable discussing treatment options.

A critical aspect of a radical prostatectomy is tailoring it to the individual features of each man's cancer. One size does not fit all. This means the exact same procedure is not appropriate for every person. The location, size, and other features of the cancer are considered to design an operation that is appropriate for the person.

A radical prostatectomy is very complex and requires a high level of technical precision.

In a laparoscopic radical prostatectomy, a surgeon inserts a tiny camera called a laparoscope through a small cut in the abdomen. The camera gives doctors a magnified, high-definition picture of the prostate gland. With that image as a guide, the surgeon can remove the prostate, seminal vesicles, and lymph nodes using special tools.

To do a robot-assisted procedure, a surgeon sits at a console that has a screen as well as hand, finger, and foot controls. The surgeon's hand, wrist, finger, and foot movements control the robotic instruments inside the patient in real time.

The robot is really just a very sophisticated surgical tool. The most important factor in a successful surgery is the skill and experience of the surgeon, working with the tool that he or she is most comfortable with. The main objective of any cancer operation — no matter how it is done — is to get all of the cancer out and get it out safely.

What should people know about the potential complications or side effects from a radical prostatectomy?
A radical prostatectomy is very complex and requires a high level of technical precision. The prostate is surrounded by nerves and structures that are important to normal urinary and sexual function. Men who have this procedure are understandably concerned about the possibility of complications that affect longer-term quality-of-life issues. These can include urinary control, also called urinary continence, and changes in sexual function.

Over the past few decades, technical refinements have dramatically reduced the number of complications with this surgery. We look for ways to use the results of imaging tests when planning a surgery. Then we can avoid injuring important structures, which minimizes the risk of incontinence and maximizes the

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chance of maintaining sexual function. We continue to look for ways to further minimize the risk of side effects.

Studies have shown that patients of surgeons who regularly perform radical prostatectomies have fewer complications on average than those who do these surgeries less often. I myself have performed more than 3,000 radical prostatectomies. The other MSK surgeons also have vast experience in this procedure.

It's always a balance between removing the cancer and trying to preserve function. The balance is different for each person because each cancer is different. People need to ask questions and be clear about their expectations.

Seek out experts who can help guide men with prostate cancer in regaining their urinary and erectile function.

Ultimately, it's about finding a surgeon with whom you feel comfortable, someone who sets realistic expectations based on your situation.

By Jim Stallard,
Wednesday, June 13, 2018

https://www.mskcc.org/blog/prostate-cancer-surgery-what-you-should-know

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Researchers Have Identified a New Subtype of Prostate Cancer

Researchers have identified a new subtype of prostate cancer that occurs in about 7% of patients with advanced disease. This subset of tumours were responsive to immunotherapy treatment.

The subtype is characterised by loss of the gene CDK12, writes the researchers. It was found to be more common in metastatic prostate cancer compared to early-stage tumours that had not spread.

Tumours in which CDK12 was inactivated were responsive to immune checkpoint inhibitors, a type of immunotherapy treatment, that has overall had limited success in prostate cancer.

"Because prostate cancer is so common, 7% is a significant number. The fact that immune checkpoint inhibitors may be effective against this subtype of prostate cancer makes it even more significant," said Dr. Arul Chinnaiyan, Director of the Michigan Center for Translational Pathology and senior author of the study.

"This is an exciting prospect for patients who have CDK122 alterations and may benefit from immunotherapy," he added.

In this study, published in Cell, researchers looked at DNA and RNA sequencing data from 360 tumour samples from patients with metastatic castration-resistant prostate cancer. This is an aggressive, advanced form of the disease in which the cancer has spread throughout the body and no longer responds to traditional hormone-based treatments.

Tumour samples were from University of Michigans ONCOSEQ program, and from samples collected through the Stand Up to Cancer-Prostate Cancer Foundation Dream Team.

What the researchers found, was a loss of CDK12 in only about 1% of early prostate cancer samples. That jumped to 7% for metastatic cancer, which indicates a more aggressive form of the disease.

"It suggests that those early-stage patients who have CDK12 loss are the ones who will develop metastatic disease. This could be a harbinger in early cancer," Chinnaiyan said.

By following the mechanism of how CDK12 loss impacts the cell, researchers found a process in which cells create neoantigens that are foreign to the immune system. This boosts immune fighting T-cells, which may explain why these patients benefit from immune checkpoint blockade.

This suggests that a precision medicine approach to prostate cancer could help better direct immunotherapy treatment, as well as explain why some prostate cancer patients have had exceptional responses to immunotherapy while the treatment has had lacklustre results overall in prostate cancer.

The team had first recognised a possible role for CDK12 in a 2015 paper that evaluated the genomic landscape of advanced prostate cancers. CDK12 has also been linked to ovarian cancer.

Little is known about CDK12 on a molecular basis, but scientists do know that CDK12 regulates several critical cellular processes and is essential for development.

Eliminating it is likely lethal to most cell types. So why can tumours lose CDK12 and survive? Researchers suspect cancer must inherit something that allows it to grow in the face of CDK12 loss. More study is needed to understand this.

"This very promising study suggests that CDK12 loss may be a biomarker for identifying prostate cancer patients who may respond to checkpoint immunotherapy," commented Dr. Howard Soule, Executive Vice President and Chief Science Officer of the Prostate Cancer Foundation.

…"using this information to identify new classes of precision treatments that can be used to improve the lives of men with prostate cancer," he added.

June 18, 2018 Frida Holme

http://www.frontlinegenomics.com/news/23923/researchers-have-identified-a-new-subtype-of-prostate-cancer/

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Common Prostate Cancer Treatment May Double Dementia Risk

In a recent study, researchers from Penn Medicine find that a common hormone therapy to treat prostate cancer may double a man's risk of dementia, regardless of his age.

The Penn Medicine study is published in JAMA Oncology.

Androgens (male hormones) normally play a key role in stimulating prostate cell growth. Therapies that suppress androgen production or activity are often used in treating prostate tumors.

However, researchers find that drastically reducing androgen activity can have adverse side-effects.

Previous studies have found links between low testosterone levels and obesity, diabetes, high blood pressure, and heart disease. All these conditions are known risk factors for dementia.

Recently, researchers discovered a dramatic association between Alzheimer's disease and androgen deprivation therapy (ADT).

ADT is a mainstay of treatment for prostate cancer since the 1940s currently used in over half million men in the United States.

Research in recent years also has linked ADT and low testosterone to cognitive deficits and has shown that men with Alzheimer's tend to have lower testosterone levels, compared to men of the same age who don't have the disease.

However, it is currently unknown if ADT may contribute to the risk of dementia.

In the study, the team compared the medical records of almost 9,500 prostate cancer patients who received ADT vs. those who did not.

The finding of the study showed that the ADT group, compared to the control group, had significantly more cases of dementia in the years following the initiation of ADT.

The absolute increased risk of developing dementia was 4.4% at five years: 7.9% among those who received ADT vs 3.5% in those who did not, which is more than double the risk. The results were statistically significant.

The analyses also suggested a "dose-response effect." Patients who had been receiving ADT for at least 12 months had the greatest risk of dementia, they found.

There was also no evidence of an interaction between use of ADT and age. The risk was doubled in both age groups.

The probability of developing dementia at five years was 13.7% in men over 70 who had ADT vs. 6.6% in men over 70 who did not.

For men younger than 70, it was 2.3% in those who had the therapy vs. one percent for those who did not.

While the study does not prove that ADT increases the risk of dementia, it does strongly supports that possibility.

There are several plausible mechanisms that may explain the association between ADT and dementia.

There is some evidence that testosterone has a general protective effect on brain cells, so that lowering testosterone would leave the brain less able to resist the processes leading to dementia and Alzheimer's.

June 17, 2018Source: Penn Medicine

https://ihealthliving.com/2018/06/common-prostate-cancer-treatment-may-double-dementia-risk/

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New Prostate Cancer Radiotherapy Technique Aims to Preserve Sexual Function

June 18, 2018 — A multicenter clinical trial being led by UT Southwestern physicians is testing a technique for sparing nerve bundles and arteries involved in sexual function to preserve potency in patients getting radiation therapy for prostate cancer.

"Nowadays, mortality after treatment for localized prostate cancer is as low as 1 percent at 10 years," said Neil Desai, M.D., assistant professor of radiation oncology, a Dedman Family Scholar in Clinical Care, and principal investigator of the POTEN-C trial. "By contrast, as many as half of all patients being treated for prostate cancer will experience some decline in sexual function. It is appropriate, therefore, that our focus has shifted to this aspect of quality of life."

The new technique being tested

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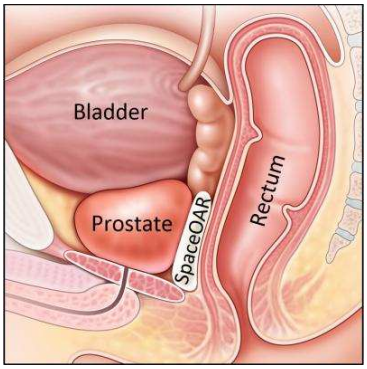
involves reducing the dose of radiation on one side of the prostate, where imaging shows no cancer, in order to spare nerves and blood vessels on that side. To achieve this goal, patients in the study will be treated with a highly precise form of radiation called stereotactic ablative radiotherapy (SAbR), and a spacer gel (SpaceOAR) will be placed between the rectum and prostate, which may help reduce the radiation dose to nerve bundles involved in sexual function. Half the patients in the study will be randomly assigned to the new radiation technique with reduced dosage on one side and half will receive standard SAbR.



Kevin Stanfield of Mount Vernon, Texas, said he became a detective, scoping out all the options – watch-and-wait surveillance, surgery, radiation – when he learned he had prostate cancer, which had taken his grandfather's life. Radiation and participation in the POTEN-C trial were the options Stanfield chose.

"The potency was a big deal," said Stanfield. "It's not that I'm some sort of Romeo or anything, but my wife is a few years younger than me. We enjoy our time together."

Stanfield will be one of 120 patients enrolled in the study, which will include patients at up to nine major medical center sites. All patients in the study will be followed for two years. UT Southwestern will lead the clinical trial.

The POTEN-C trial builds on prior work done at UT Southwestern Medical Center,.

Robert Timmerman, M.D., professor of radiation oncology and neurological surgery, has been at the forefront of national efforts to advance stereotactic ablative radiotherapy, or high-intensity, high-precision radiation therapy in prostate cancer. SAbR means fewer radiation treatments for patients as well as less damage to healthy tissue, and it has become standard treatment in many situations. Timmerman holds the Effie Marie Cain Distinguished Chair in Cancer Therapy Research.

UT Southwestern also was part of clinical trials proving the value of the biodegradable spacer gel SpaceOAR that is used to protect the rectum from damage during radiation treatment for prostate cancer.

The POTEN-C trial incorporates both prior projects, culminating in what Desai hopes will be a way to reduce the burden of therapy on men and their partners. "We're using advances in MRI [magnetic resonance imaging] to locate the disease, the SAbR technique's precision, and now the SpaceOAR gel to plan a new approach to reducing sexual dysfunction. We are excited to be able to combine the results from the last 10 years of research to improve the outlook for our patients who require prostate cancer treatment."

Stanfield said he realizes as a participant in a blinded randomized study, there's no guarantee he will get the nerve bundle-sparing technique, but that does not bother him. "I might get the new treatment or I might not; however, if I don't I will still get the best that's available now. I'm really excited about being a part of this," he said.

"Basically, we're trying to give men more choices, trying to preserve their potency up front. If this ends up being a positive trial, it's a pretty big deal for our field," Desai said.

The POTEN-C trial is funded by Augmenix, the maker of SpaceOAR gel.

For more information: www.augmenix.com

https://www.itnonline.com/content/new-prostate-cancer-radiotherapy-technique-aims-preserve-sexual-function

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"You Can Help Spread The Word About Prostate Cancer"

Prostate cancer is one of the most common cancers in men. Discovered early, it can be successfully treated in the majority of cases. Such early discovery is dependent on men being aware of the facts about this disease and getting checked. *Early discovery saves lives.*

To help raise awareness and encourage "getting checked" the Manitoba Prostate Cancer Support Group is happy to provide speakers to make presentations to interested groups in the community. There is no charge for this service and the size of the group doesn't matter. If you are involved with a group that would like to learn more about prostate cancer, and perhaps save some lives in the process, please contact Pat Feschuk (tel: 204-654-3898; email: lizpat@shaw.ca). *Remember that if a man has prostate cancer the sooner he learns about it the better. Not knowing about it simply allows it to grow and spread.* **So do something about it** ….. help spread the word.

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FUTURE MEETINGS 2018

15 Aug. Speaker: Dr. Piotr Czaykowski
Title: "Prostate cancer, you and CancerCare Manitoba"

19 Sept. This is our highlight event of the year!

This year we will focus on the changes which have transformed prostate cancer treatment through the years and what the future may bring. Dr. Darrel Drachenberg will deliver the keynote address on this theme and will answer questions from the audience.
Mark your calendar and be there!
(Note that the September meeting location is at the Caboto Centre, 1055 Wilkes Ave, Wpg)

All meetings (except September) will be held at :
The First Unitarian Universalist Church of Winnipeg,
603 Wellington Crescent

All meetings are 7 – 9 pm.
(First hour for general discussion;
second hour for expert guest speaker)

Everyone Welcome Plenty of free parking

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