

STAMPEDE trial results on docetaxel, zoledronic acid and celecoxib for prostate cancer

Summary

Men who took part in STAMPEDE:

- had high-risk prostate cancer, or prostate cancer that had already spread to the nodes or other parts of the body
- were starting long-term hormone therapy for the first time
- were fit enough to have chemotherapy

It compared several treatments to the standard treatment used for prostate cancer (see diagram below).

STAMPEDE found no difference in how long, on average, men who had **zoledronic acid** in addition to the standard treatment lived, compared to those who had the standard treatment alone.

STAMPEDE found that men who had **docetaxel** in addition to standard treatment on average

lived 10 months longer than men who had standard treatment alone. They also had more time before their disease got worse. We can be more certain for the sub-group of men whose disease had already spread to distant parts of their body. Men who had docetaxel were more likely to have severe short-term side-effects. One in two men who had docetaxel and standard treatment had at least one severe side-effect, compared to one in three men who had standard treatment alone.

STAMPEDE found no difference in how long, on average, men who had **celecoxib** and the standard treatment lived, compared to those who had the standard treatment alone.

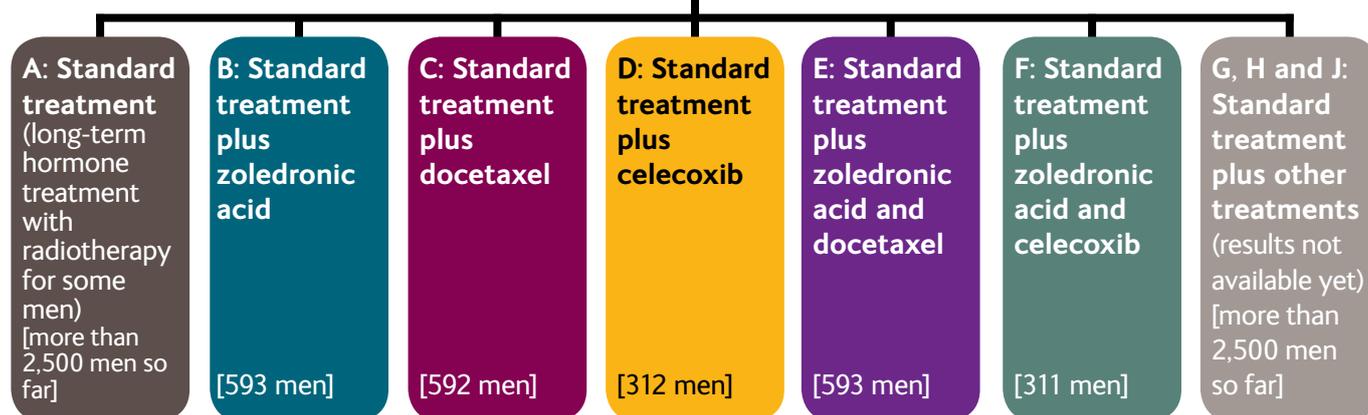
STAMPEDE found that men who had both **zoledronic acid and docetaxel** added to the standard treatment, on average, lived 5 months longer than men

who had the standard treatment alone. This improvement is smaller than the improvement seen from adding just docetaxel to standard treatment. One in two men who had zoledronic acid, docetaxel and standard treatment had at least one severe side-effect, compared to one in three men who had standard treatment alone.

STAMPEDE also found that men who had both **zoledronic acid and celecoxib** added to standard treatment lived, on average, 6 months longer than those who had the standard treatment alone. But we do not have enough evidence to be sure this difference was not due to chance. We can be more certain for the sub-group of men whose disease had already spread to distant parts of their body. The number who reported severe side-effects was similar to those who had just the standard treatment (one in three).

Thank you for taking part in the STAMPEDE trial.

Men who agreed to take part in the trial were randomly put into one of several groups:



Thank you for taking part in the STAMPEDE trial

You and other volunteers are helping researchers answer important health questions. Here we describe the results of this study so far.

We wrote this summary in January 2016. Newer information may have emerged since we wrote it. This summary includes only results from STAMPEDE. Other studies may find different results.

The STAMPEDE trial is looking at several new ways to treat prostate cancer. We now have results from five of these approaches. These approaches used the drugs zoledronic acid, docetaxel and celecoxib alongside standard treatment.

Study information

The study included men who:

- had high-risk prostate cancer, or prostate cancer that has already spread to the nodes or other parts of the body
- were starting long-term hormone therapy for the first time
- were fit enough to have chemotherapy

The study started in 2005. It included men at hospitals throughout the UK and Switzerland.

This study compared several new treatments to the standard treatment used for prostate cancer:

- A. Standard treatment (long-term hormone treatment, with radiotherapy for some men)
- B. Standard treatment plus zoledronic acid (a drug used to reduce bone problems in men whose cancer has spread to their bones)
- C. Standard treatment plus docetaxel (a chemotherapy drug)
- D. Standard treatment plus celecoxib (an anti-inflammatory drug)
- E. Standard treatment plus zoledronic acid and docetaxel
- F. Standard treatment plus zoledronic acid and celecoxib

It is a Phase III randomised controlled trial. This means that it involved a large number of patients, and was designed to test how well the new treatments work. We looked at whether men who were given any of these drugs in addition to the standard treatment lived longer, on average, to those who had the standard treatment alone. We also looked at whether adding these drugs delayed the disease getting worse.

Results

The average age of men joining the trial was 65 years. Six in every 10 men taking part had cancer that had already spread to distant parts of their body. The results are averages for the particular people studied and cannot be assumed to be true for every individual. Not all participants in each part of the study had the same results. Not every man who took part in the trial reported side-effects. The most common severe side-effects are discussed in each of the results section that follows.

Group A: Standard treatment

The standard treatment was long-term hormone treatment, with radiotherapy for some men.

How did these men do?

Half the men who had just the standard treatment lived for at least 5.9 years after joining the trial. 55% of men who had the standard treatment alone were alive 5 years after joining the trial.

28% of men in this group made it to five years from joining the trial without their disease getting worse. Half the men who had just the standard treatment lived for at least 2.9 years before their disease got worse.

What were the side-effects?

Around one in every three men who received the standard treatment (hormone therapy, plus radiotherapy for some men) had at least one severe side-effect. The common severe side-effects (ones that at least one in every twenty men had) were:

- Impotence and/or hot flushes
- Bone pain or generalised pain
- Kidney problems or urinary tract infections

Group B: Standard treatment plus zoledronic acid

Zoledronic acid was given through a drip once every three weeks for six cycles, then once every four weeks for up to two years.

How did these men do?

Adding zoledronic acid to standard treatment did not improve how long men with prostate cancer lived, compared with those who had just standard treatment. 57% of men who had zoledronic acid plus the standard treatment were alive 5 years after joining the trial. This is slightly higher than the 55% seen in men who had the standard treatment alone, but the difference is not big enough for us to be sure it was not due to chance.

31% of men in this group made it to five years from joining the trial without their disease getting worse. But this is only slightly higher than in the standard treatment arm, and the difference is not big enough for us to be sure it was not due to chance.

What were the side-effects?

Men who had zoledronic acid had similar side-effects to those who had just the standard treatment. Around one in every three men who had zoledronic acid as well as standard treatment had at least one severe side-effect. The common severe side-effects (ones that at least one in every twenty men had) were:

- Impotence and/or hot flushes
- Tiredness, fever, or weakness
- Bone pain or generalised pain
- Kidney problems or urinary tract infections

Group C: Standard treatment plus docetaxel

Docetaxel was given through a drip once every three weeks for six cycles. Men in this group also had a drug called prednisolone or prednisone once a day, and standard drugs used to help patients have their chemotherapy.

How did these men do?

For the whole group, on average, men who had docetaxel lived 10 months longer than men who had standard treatment alone. 63% of men who had docetaxel plus standard treatment were alive 5 years after joining the trial, compared to 55% who had standard treatment alone.

The evidence is strong for men whose disease had already spread to other parts of their body. Those men who had docetaxel as well as standard treatment lived 15 months longer than similar men who had just the standard treatment.

We do not yet have enough evidence for men whose disease had not spread to distant parts of their body. We cannot be sure that those who had docetaxel lived longer. We are continuing to follow-up these men, so hope to be able to answer this question in the future.

On average, men who had docetaxel lived for 3.7 years before their disease got worse. This

was 9.4 months longer than those who had just the standard treatment. 38% of men in this group made it to five years from joining the trial without their disease getting worse. This evidence is strong for both men whose disease had spread and those whose disease had not spread to distant parts of their body.

What were the side-effects?

Men who had docetaxel in addition to standard treatment were more likely to have a severe side-effect than those who had just the standard treatment. Around half of men who had docetaxel had at least one severe side-effect. The common severe side-effects (ones that at least one in every twenty men had) were:

- Infection because of weakened immune system
- Low numbers of white blood cells
- Impotence and/or hot flushes
- Diarrhoea, stomach ache, constipation, sickness
- Tiredness, fever, or weakness
- Bone pain or generalised pain
- Breathlessness, cold/flu

The side-effects from docetaxel were short-term, and generally stopped once treatment with docetaxel was finished.

Group D: Standard treatment plus celecoxib

Celecoxib was taken as a tablet twice a day for up to one year.

How did these men do?

Men who had celecoxib plus standard treatment did not live longer, on average, than the group who had just standard treatment.

What were the side-effects?

Men who had celecoxib and standard treatment had similar side-effects to those who had just the standard treatment. Around one in every three men who had celecoxib as well as standard treatment had at least one severe side-effect. The common severe side-effects (ones that at least one in every twenty men had) were:

- Impotence and/or hot flushes
- Bone pain or generalised pain

Group F: Standard treatment plus zoledronic acid and celecoxib

How did these men do?

On average, men who had zoledronic acid and celecoxib lived 6 months longer than those who had the standard treatment alone. 4% more were alive five years after joining the trial. But we do not have enough evidence to be sure this difference was not due to chance. We can be more certain for the sub-group of men whose disease had already spread to distant parts of their body.

This is the first trial to show that men with disease that has spread who have this combination live longer than those who have standard treatment. We need more research to confirm this finding.

What were the side-effects?

Men who had zoledronic acid, celecoxib and standard treatment had similar side-effects to those who had just the standard treatment. Around one in every three men who had celecoxib and zoledronic acid as well as standard treatment had at least one severe side-effect. The common severe side-effects (ones that at least one in every twenty men had) were:

- Impotence and/or hot flushes
- Bone pain or generalised pain
- Kidney problems or urinary tract infections
- Diarrhoea, stomach ache, constipation, sickness

Group E: Standard treatment plus zoledronic acid and docetaxel

How did these men do?

On average, men who had zoledronic acid and docetaxel lived 5 months longer than men who had the standard treatment alone. 60% of men who had zoledronic acid and docetaxel were alive 5 years after joining the trial, compared to 55% who had standard treatment alone. But the improvement seen from this combination is smaller than the improvement seen from adding just docetaxel to standard treatment.

On average, men who had zoledronic acid and docetaxel lived for 3.6 years before their disease got worse. This was 8.3 months longer than those who had just the standard treatment. 34% (one in three) of men in the zoledronic acid and docetaxel group made it to five years from joining the trial without their disease getting worse.

What were the side-effects?

Men who had docetaxel with zoledronic acid in addition to standard treatment were more likely to have a severe side-effect than those who had just the standard treatment. Around half of men who had docetaxel and zoledronic acid in addition to standard treatment had at least one severe side-effect. The common severe side-effects (ones that at least one in every twenty men had) were:

- Infection because of weakened immune system
- Low numbers of white blood cells
- Tiredness, fever, or weakness
- Impotence and/or hot flushes
- Bone pain or generalised pain
- Diarrhoea, stomach ache, constipation, sickness
- Kidney problems or urinary tract infections

The additional side-effects in this group were short-term, and generally stopped once treatment with docetaxel was finished.

What else has STAMPEDE found out?

STAMPEDE is also helping us to answer other questions. Because STAMPEDE is so big, we can compare other aspects of treatment that were not randomised.

One example is whether men whose cancer has spread to nearby lymph nodes should have radiotherapy. Doctors did not know whether radiotherapy helps these men. We used data from STAMPEDE to compare how well men whose disease had spread to nearby lymph nodes who were planned to have radiotherapy did, compared to those who were not planned to have radiotherapy. We found that those men who were planned to have radiotherapy lived, on average, for longer without their disease getting worse than those who were not planned to receive radiotherapy.

Because of this new evidence, doctors are now using radiotherapy more for men whose disease has spread to nearby lymph nodes.

What does this mean for you?

These results do not change your treatment or follow-up if you are already part of STAMPEDE.

Please do carry on coming to your appointments. We are still very interested in how you do. This information will be useful to answer questions about long-term effects.

Through taking part in STAMPEDE you have helped other men with prostate cancer.

Final comments

Thank you for taking part in STAMPEDE. This research helps future patients and families by helping us to understand more about each drug we are studying.

We have found that men who receive docetaxel in addition to standard treatment live longer than men who have standard treatment alone. This result is changing how men with prostate cancer are treated.

STAMPEDE is continuing to follow-up men in the groups for which we now have results. It is also looking at other questions.

We do research to try to find the best ways to help patients, and you helped us to do that.

Thanks again for being part of this study.

What does this mean for the STAMPEDE trial?

The STAMPEDE trial is still going on because we have added other questions to the trial since the original groups started:

- G. Standard treatment plus abiraterone – we now have enough men in this group, and expect results in 2017
- H. Standard treatment plus radiotherapy to the prostate for men whose disease has spread to distant parts of their body – we are continuing to add new men to this group
- J. Standard treatment plus enzalutamide and abiraterone – we are continuing to add new men to this group
- K. Standard treatment plus metformin (a drug that is used to treat diabetes) – this group is opening in 2016

There are also several other questions we would like to add to the STAMPEDE trial. We expect to add new groups to STAMPEDE over the next few years.

We think that the results from STAMPEDE show that docetaxel should become part of the standard treatment for men who are fit enough to have it. Because of this, men offered docetaxel as part of their standard treatment are still able to join STAMPEDE, regardless of which group they get allocated.

Further information

This study is officially known as STAMPEDE: Systemic Therapy in Advancing or Metastatic Prostate Cancer: Evaluation of Drug Efficacy (MRC PR08). It is registered on clinical trials databases, where you can find out more information.

We are using findings from this study to inform doctors about a new way to treat people with prostate cancer. NHS England have updated their guidance to include the new evidence from STAMPEDE.

The Medical Research Council is the sponsor for this study. It is funded by Cancer Research UK, the Medical Research Council, Astellas, Janssen, Novartis, Pfizer and Sanofi-Aventis.

If you have questions about STAMPEDE, please talk to your study doctor or research nurse.

This research is important. Thank you for helping us to understand more about how to treat prostate cancer.

Links

Trial registration details:

- [ISRCTN78818544 \(www.ISRCTN.com\)](http://www.ISRCTN.com)
- [NCT00268476 \(www.ClinicalTrials.gov\)](http://www.ClinicalTrials.gov)
- EUDRACT: 2004-000193-31

To learn more about this study, visit www.stampededtrial.org or <http://bit.ly/STAMPEDEtrial>

You can read more about these results using these links:

- Docetaxel and zoledronic acid results <http://bit.ly/STAMPEDEresults>
- Celecoxib results <http://bit.ly/STAMPEDEcelecoxib>

This film explores the docetaxel and zoledronic acid results

<http://bit.ly/STAMPEDEfilm>

If you would like to read the full scientific papers, these are available:

- Docetaxel and zoledronic acid results (published in The Lancet): <http://bit.ly/STAMPEDELancet>
- Radiotherapy for men whose disease has spread to their lymph nodes <http://bit.ly/STAMPEDEnode>

For more information about clinical trials, visit <http://bit.ly/abouttrials>