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Before the Senate Committee on Foreign Relations

The Al-Megrahi Release: One Year Later

September 29, 2010

Mr. Chairman, distinguished members of the Foreign Relations Committee, it is my privilege to come before you today to provide my expert opinion about the "three months to live" prognosis Scottish physicians gave Abdelbaset Ali Mohmed al-Megrahi in August 2009.

Based on the medical report issued by the Scottish authorities, I believe that three month prognosis was medically unjustifiable. Any physician with any training or experience in treating prostate cancer would have known that a three month prognosis simply could not be made based on Mr. al-Megrahi's clinical situation at the time of diagnosis, the treatment received and the response to that treatment. Moreover, medical anomalies regarding his care – especially the use of chemotherapy – call into question how the three month prognosis was determined.

Qualifications

I base my assessment today on a long history of training, practical experience, and in-depth research in the field of prostate cancer. I earned my medical degree from the Medical College of Georgia and competed residency training in Surgery and Urology at the University of Kentucky Medical Center and a research fellowship in Urologic Oncology at the Johns Hopkins University School of Medicine. I am licensed by New York and North Carolina, a Diplomat of the National Board of Medical Examiners and the American Board of Urology, and a Fellow of the American College of Surgeons.

My clinical practice focuses upon prostate cancer and robot-assisted laparoscopic surgery. My laboratory research focuses upon the role of the androgen receptor (the protein that binds male hormones to activate growth) in racial differences in prostate cancer aggressiveness and prostate cancer recurrence during androgen deprivation therapy, hereafter called hormone treatment. I have authored or co-authored 206 publications and book chapters and a book "Androgen Action in Prostate Cancer." I serve on the editorial boards of The Prostate, Journal of the National Comprehensive Cancer Network, Therapeutic Advances in Urology, and Hormones and Cancer, and I review for several journals including Cancer, Cancer Research, Clinical Cancer Research, Journal of Clinical Oncology, Journal of Urology, and Urology.

I also am the Associate Director and Senior Vice President for Translational Research, Chair of the Department of Urology, Founder of the Prostate Program, and Professor of Oncology, at Roswell Park Cancer Institute, Professor of Urology at the University at Buffalo School of

Medicine and Biomedical Sciences, and Adjunct Professor of Surgery and Member, UNC-Lineberger Comprehensive Cancer Center at University of North Carolina.

I also bring to your attention that I am Chair of the National Comprehensive Cancer Network (NCCN) Guidelines Panel for Prostate Cancer, Vice-Chair of the Genito-Urinary Committee and Chair of the Genito-Urinary Surgery Subcommittee, Cancer and Leukemia Group B (CALGB), and Past-President of the Society for Basic Urologic Research. I am a member of the American Medical Association, American Association for the Advancement of Science, American Association for Cancer Research, American Urological Association and American College of Surgeons.

The Prognosis of Mr. al-Megrahi

According to the medical report released by Scottish authorities, Mr. al-Megrahi was diagnosed September 2008 with poorly differentiated (Gleason grade 4+5=9 on a scale of 2 [best] to 10 [worst]), bone metastatic prostate cancer and he had a PSA of 363 ng/ml (normal < 2.5 ng/ml). In layman's terms, this means he was diagnosed with an incurable prostate cancer that was so advanced it had spread to his bones.

Fortunately for Mr. al-Megrahi, advanced prostate cancer can be put into remission in almost all men by starving the cancer of the male hormones it needs to grow and spread. He began hormone treatment, which is the standard treatment for advanced prostate cancer, in September or October 2008.

Mr. al-Megrahi had an initial response to this treatment, and his PSA dropped to 12.0 ng/ml. In other words, he responded but the failure of his PSA to fall to normal (<2.5 ng/ml) or undetectable (<0.2 ng/ml) predicted a remission that would be shorter than average .

Unfortunately for Mr. al-Megrahi, his cancer recurred in spite of hormone treatment in April 2009 when his PSA rose to 22.1 ng/ml and then 45.1 ng/ml. In short, the hormone treatment was failing and his PSA continued to rise, eventually reaching 208.8 July 2009. This sequence of PSA test values follows a PSA doubling time of approximately 2 months, which is consistent with a very rapidly growing prostate cancer. Up until this point, Mr. al-Megrahi's treatment was standard care.

Mr. al-Megrahi was released August 20, 2009 based on a medical prognosis that was determined on or before August 10, 2009. We know this because that was the date of the medical report, prepared by a Scottish physician named Dr. Andrew Fraser, which was the medical basis for Mr. al-Megrahi's release. Scottish officials based his compassionate release on the fact that, according to this report, he was believed to have three months or less to live. In my 23 years of experience caring for more than 2000 prostate cancer patients and reading

clinical studies that evaluated thousands of patients in similar conditions, there is no conceivable way a cancer specialist or anyone familiar with the treatment of prostate cancer could have given a three month prognosis based on the clinical situation and treatment described above. Let me explain why:

- A patient with prostate cancer with an accurate three month prognosis would have to be almost bedridden. Dr. Fraser noted in his final medical report that Mr. al-Megrahi's cancer "did not restrict or remove (his) ability to carry out any particular tasks." That is not the definition of a patient with prostate cancer who will die within three months. Also, as could be seen by the footage of his reception in Libya, he was ambulatory upon his arrival in Libya.

- We know that Scottish Government authorities, doctors, and Mr. al-Megrahi himself all claimed that Mr. al-Megrahi planned on taking courses of chemotherapy. However, a patient with prostate cancer with an accurate three month prognosis would have to be so ill that he would have been unable to receive a regimen of chemotherapy. A patient with prostate cancer with an accurate three month prognosis would instead be given palliative or end-of-life care focused on pain management and making the patient as comfortable as possible.

- Building on the two previous points, a prognosis of three months survival cannot be made until either all standard treatment options like chemotherapy have been attempted and evaluated or the patient has clear symptoms – like an inability to walk – that make it medically unreasonable to explore further treatment. In Mr. al-Megrahi's case, they hadn't even begun chemotherapy but intended to do so, which clearly indicates that he was physically able to undergo the next course of treatment and was not within three months of dying.

Contrary to documents published by the Scottish Government, I now understand that Mr. al-Megrahi received chemotherapy in Scotland just prior to his release. In July 2009, Dr. Andrew Fraser said that "different treatment options had been discussed, and a new treatment had been embarked upon." This new treatment apparently was chemotherapy, as stated by George Burgess, the Scottish former Deputy Director for Criminal Law and Licensing, in a meeting with Senator Menendez's staff. I'll explore what that would mean for Mr. al-Megrahi's life expectancy, but first I note that it takes at least six weeks to evaluate the effectiveness of chemotherapy after starting the treatment. If Mr. al-Megrahi began his chemotherapy in July 2009 after his hormone treatment failed, six weeks would not have passed prior to the final prognosis issued on or before August 10, 2009.

Still, let us explore what happens when patients just like Mr. al-Megrahi – a patient who had failed hormone treatments and who had similar symptoms – receive chemotherapy. There are published and readily known studies from 2004 that enrolled men with recurrent prostate cancer that proved that using the chemotherapy drug, docetaxel (Taxotere™), an every 3 week outpatient regimen, reduced pain and extended survival. These were men who had failed hormone treatment but were well enough to undergo chemotherapy, just like Mr. al-Megrahi. These men survived an average of 17 or 19.2 months from the start of chemotherapy. Another study of 1296 men on 7 different studies, of whom some received chemotherapy and others received less effective treatment, showed their average lifespan was 13.3 months. Today, men have many other options even after they fail hormone treatment and chemotherapy. Their recurrent prostate cancer can be managed with other forms of hormone treatment, such as ketaconazole, prednisone, or DES patches. Mitoxantrone, a weaker chemotherapy, can reduce symptoms but, unlike docetaxel, does not extend survival, or painful bone metastases can be treated with radiation.

Finally, Mr. al-Megrahi may benefit from any of 3 classes of new drugs, 1) immunotherapy with sipuleucel-T (Provenge™), 2) better drugs that block production of strong male hormones from weak male hormones, such as abiraterone, TAK-700, or VN124-1, or 3) a new small molecule, MDV3100, which blocks the androgen receptor better than the anti-androgen Mr. al-Megrahi received. Abiraterone was discovered in London and new evidence from a large trial in the United States suggests that it extends life in men like Mr. al-Megrahi.

In other words, Mr. al-Megrahi had many treatment options available to him in August 2009 that would have extended his life, on average, at least another year, and more likely 2 years or more.

In short, ladies and gentlemen, I am not the *least* bit surprised that Mr. al-Megrahi is alive. And it should come as absolutely no surprise to the cancer specialists who cared for Mr. al-Megrahi either.

Conclusions

Mr. al-Megrahi's release on compassionate grounds appears to have erred in two fundamental ways. First, we now know that Mr. al-Megrahi received chemotherapy in Scotland, which Scottish cancer specialists would have known was going to extend his life on average 17 or 19.2 months, depending on which of these well done, large, well known studies you wish to consider. Even if Mr. al-Megrahi didn't receive chemotherapy in Scotland and he was just *planning* on receiving such, he would still live on average 17 or 19.2 months beyond the starting date when he *did* receive chemotherapy upon his return to Libya. Again, Scottish cancer specialists would have known this from medical research dating from 2004.

The second reason his release appears to have erred was because his health was inconsistent with a patient with an accurate prognosis of three months survival. For instance, he was not bed-ridden.

Some may speculate that Mr. al-Megrahi's failure of hormone treatment meant that his cancer was particularly aggressive and therefore his prognosis was worse than others who responded more favorably to hormone treatment. That is true; many men have long remissions from hormone treatment but he didn't. However, his prostate cancer's rapid growth rate during hormone treatment paradoxically made a response to chemotherapy all the more likely, since chemotherapy works best against rapidly dividing cells. In short, patients with aggressive prostate cancer like Mr. al-Megrahi respond *better* to chemotherapy than those patients with a less aggressive prostate cancer.

Therefore, I am not at all surprised that he may be alive more than 14 months after beginning chemotherapy and/or other treatments (such as abiraterone) for his rapidly growing, recurrent prostate cancer. I also believe that any physician with training and experience in prostate cancer would find a three month prognosis for a patient in Mr. al- Megrahi's condition difficult to believe and possibly even ridiculous.

Thank you for this opportunity to address the inconsistencies apparent in Mr. al-Megrahi's compassionate release from prison.

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10. Standard of care for recurrent prostate cancer - chemotherapy – can be found in the NCCN Prostate Cancer Guidelines (www.nccn.org/members; see PROS-7 System Therapy).

11. The survival of men with recurrent prostate cancer can be estimated using a nomogram (https://www.calgbapps.org/Nomogram/CRPCv1p1.html) that estimates 12, 18 and 24 months survival probability using 7 variables, which include presence of visceral disease, Gleason score, performance status, PSA at diagnosis, LDH, alkaline phosphatase and hemoglobin.