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# Treatment with Progesterone Receptor Modulators, E.G., Mifepristone May Provide Marked Palliation and Increase Longevity in People with Advanced Cancers (Including Those Devoid of the Classic Progesterone Nuclear Receptor) by Inhibiting the Intracytoplasmic Production of a Key Immunosuppressive Protein Known as the Progesterone Induced Blocking Factor

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## Statement of the Problem

The progesterone induced blocking factor (PIBF) is an immunomodulator 757 amino acid protein, not present in normal cells, but unique to rapidly proliferating cells, e.g., fetal placental cells (mesenchymal, embryonic and trophoblastic cells), and in various cancer cells. The nuclear PIBF protein, which affects cell-cell regulation, is cleaved into intracytoplasmic splice variants (isoforms) which have significant immunosuppressive activity especially against, but not limited to, natural killer cells. Increased production of PIBF involves transmembrane progesterone receptors, and thus cancer cells devoid of the classic nuclear progesterone receptor still produce PIBF when they are at the rapidly proliferating stage. Mifepristone, a progesterone receptor modulator, suppresses intracytoplasmic PIBF. Thus it would seem prudent to determine if treatment with mifepristone can increase longevity and quality of life from cancer.

## Methodology

Mifepristone was given orally to mice with spontaneous murine cancers and to humans with advanced cancer.

## Findings

Placebo controlled murine studies found that mifepristone therapy resulted in significant increased lifespan and quality of life as determined by body conditioning scores in mice with spontaneous leukemia/lymphoma, lung, testicular and prostate cancer. For humans, compassionate use of mifepristone for patients with very advanced cancers, where no more other treatment options were available, resulted in marked prolongation of a high quality life in patients with both small cell and non-small cell lung cancer, thymic cell epithelial cancer, renal cell carcinoma, and colon cancer. Several other types of very advanced cancers demonstrated palliation following mifepristone therapy.

## Conclusion

The first patient in an investigative initiated FDA approved study who had stage IV non-small cell lung cancer with brain metastases who had failed 3 rounds of chemotherapy is leading a high quality life three years on single agent 300mg oral mifepristone. Progesterone receptor modulator should be considered for treatment of advanced cancers with no other treatment options.

## Article Information

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