Pancreatic Cancer Action Network – AACR 2012 grants program: There’s still time!

https://proposalcentral.altum.com/

Do you know any outstanding early-career researchers whom you’d like to bring (or keep) into the field of pancreatic cancer research? Applications are still being accepted for our prestigious Pathway to Leadership, Career Development, and Fellowship grants. A record high of more than $3.1 million will be distributed this year! Please click above to initiate the application process, or go to

http://www.pancan.org/section_research/research_grants_program/apply_for_a_grant.php

for eligibility requirements and information on deadlines. Spread the word! (Note: the deadline for Letters of Intent for the Innovative Grants has passed; all other mechanisms’ deadlines are October 31, 2011.)

Save the date for the AACR special conference – Pancreatic Cancer: Progress and Challenges

http://www.pancan.org/section_research/resources_for_scientists/aacr_conference_progress_and_challenges.php


Pancreatic Cancer: Progress and Challenges will take place June 18-21, 2012, in Lake Tahoe, NV. The Pancreatic Cancer Action Network is a proud lead supporter of this meeting. The conference will engage the world leaders in pancreatic cancer research and provide ample time for discussion.

Columbia lends support to the Pancreatic Cancer Research and Education Act


**2011 Gigi Shaw Arledge Conference on Pancreatic Disease**
[http://pancreasmd.org/event_20111020.html](http://pancreasmd.org/event_20111020.html)
This conference is co-chaired by Ken Olive, PhD (2011 Tempur-Pedic® Retailers – Pancreatic Cancer Action Network – AACR Career Development Award) and speakers include several grant recipients and Scientific Advisors of the organization, such as Drs. Tuveson, Bar-Sagi, Kimmelman, Petersen, and Vonderheide. The event will take place on October 20, 2011, at NewYork-Presbyterian Hospital/ Columbia University Medical Center.

** AACR releases landmark cancer progress report**
The American Association for Cancer Research released its AACR Cancer Progress Report 2011: Transforming Patient Care Through Innovation, in honor of the 40th anniversary of the National Cancer Act, calling for increased funding from the NIH and NCI.

**Pancreatic Cancer UK Study for Survival 2011**
This report garnered considerable media attention, including articles in BBC and The Lancet ([http://www.bbc.co.uk/news/health-14811010](http://www.bbc.co.uk/news/health-14811010), [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)61465-7/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)61465-7/fulltext), etc. Pancreatic Cancer UK released this report to emphasize the poor survival rate and lack of attention/funding devoted to pancreatic cancer in the UK. Among the Study for Survival Advisory Panel is Dave Tuveson, MD, PhD, Chair of the Pancreatic Cancer Action Network Scientific Advisory Board, and recipient of a 2003 Pancreatic Cancer Action Network – AACR Career Development Award.

**Surgical management of pancreatic cancer**
The Pancreatic Cancer Action Network hosted a webinar that was given by Mark Talamonti, MD, Chair of the Medical Advisory Board. The slides from this well-attended webinar are now available online.

**New York Yankees all-star pitcher David Robertson commits to strike out pancreatic cancer**
David Robertson will serve as the Honorary Captain of TEAMHOPE®, the Pancreatic Cancer Action Network’s national marathon team. His PSA ([http://www.youtube.com/watch?v=pEa_a9k_ZUI&feature=youtu.be](http://www.youtube.com/watch?v=pEa_a9k_ZUI&feature=youtu.be)) will serve to educate fans and the general public about pancreatic cancer.

**Funding opportunity: 2012 NIH Director’s Transformative Research Awards**
These grants are designed to support exceptionally innovative and/or unconventional research projects that have the potential to create or overturn fundamental paradigms. The RFA can be found at
letters of intent are due December 12, 2011, with complete applications due January 12, 2012.

NCCN/MEK inhibitor GSK1120212 – Research grant opportunity

GlaxoSmithKline, Inc has offered a $2 million research grant through the National Comprehensive Cancer Network (NCCN) to support research on the MEK inhibitor GSK1120212 in specific solid tumors, including pancreatic cancer. Studies must be NCCN investigator-initiated; collaborative studies between NCCN members are encouraged. Proposals are due by 11:59 PM EST, Thursday, November 17, 2011. Electronic submissions of proposals can begin October 15, 2011.

IU Cancer Center recruits top researcher

Murray Korc, MD will join the Indiana University Melvin and Bren Simon Cancer Center as the first Myles Brand Professor of Cancer Research. Dr. Korc was previously the scientific leader of the pancreatic cancer group at the Dartmouth-Hitchcock Norris Cotton Cancer Center in Lebanon, NH.

BIOLOGY OF CANCER

Loss of expression of the SWI/SNF chromatin remodeling subunit BRG1/SMARCA4 in IPMNs

Authors from Johns Hopkins include Jim Eshleman, MD, PhD (2011 Pancreatic Cancer Action Network – AACR Innovative Grant), Ralph Hruban, MD (Emeritus Scientific Advisory Board), and Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award and Scientific Advisory Board). This *Human Pathology* paper looks at expression of Brg1, a central component of the chromatin remodeling complex SWI/SNF regulating transcription, in intraductal papillary mucinous neoplasms (IPMNs) of the pancreas. The authors provide first evidence that Brg1 expression is lost in noninvasive cystic precursor lesions of pancreatic adenocarcinoma.

A protein therapeutic modality founded on molecular regulation

This work was partly conducted in the laboratory of Jim Eshleman, MD, PhD (2011 Pancreatic Cancer Action Network – AACR Innovative Grant). The study is also described here ([http://www.eurekalert.org/pub_releases/2011-09/jhu-pc092311.php](http://www.eurekalert.org/pub_releases/2011-09/jhu-pc092311.php)) and Dr. Eshleman is quoted. A multidisciplinary team at Johns Hopkins aimed to direct cancer treatment to the tumor, and spare normal cells, by administering a “prodrug activating enzyme”. This pro-drug is specific for cells expressing the hypoxia inducible factor HIF1a.

AGR2 is a novel surface antigen that promotes the dissemination of pancreatic cancer cells

This *Cancer Research* article includes authors Christine Iacobuzio-Donahue, MD, PhD (2007 Pancreateic Cancer Action Network Pilot Grant, Scientific Advisory Board member) and Teri Brentnall, MD (Scientific Advisory Board). The authors evaluated the role of metastasis-associated protein anterior gradient 2 (AGR2) in pancreatic cancer, and found that AGR2 was induced in all sporadic and familial pancreatic intraepithelial precursor lesions (PanINs), pancreatic ductal adenocarcinomas, circulating tumor cells,
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and metastases studied. Further, AGR2 was found to promote dissemination of pancreatic cancer cells through regulation of cathepsins B and D.

**Combined blockade of integrin α4β1 plus cytokines SDF-1α or IL-1β inhibits tumor inflammation**


Philippe Foubert, PhD (2009 Ruth Fredman Cernea – Pancreatic Cancer Action Network – Fellowship) contributed to this *Cancer Research* paper. Research out of Judy Garner, PhD’s lab at UCSD explored how the chemoattractants SDF-1α and IL-1β collaborate with myeloid cell integrin α4β1 to promote tumor inflammation and growth. They found that SDF-1α and IL-1β were highly expressed in the microenvironments of several mouse tumors, including pancreatic. Further, their data suggest that while inhibiting integrin α4β1, SDF-1α or IL-1β was sufficient to block tumor inflammation and growth, the combined blockade of these molecules greatly accentuated these effects.

**An emerging entity: Pancreatic adenocarcinoma associated with a known BRCA mutation**


This *Oncologist* study out of Eileen O’Reilly, MD (Medical Advisory Board)’s lab concludes that BRCA mutation-associated pancreatic adenocarcinoma represents an underidentified, but clinically important, subgroup of patients, particularly in regard to treatment decisions.

**EGFR essential for the development of pancreatic cancer**


The AACR issued a press release for this abstract presented at their Second International Conference on Frontiers in Basic Cancer Research held in San Francisco. Barbara Grüner from Technical University in Munich, Germany presented that deleting EGFR prior to generation of pancreatic tumors in mice led to a complete absence of PanIN lesions and only rare ductal-like lesions. The authors conclude that EGFR seems essential for induction of ADM and PanIN development in a K-Ras independent manner.

**Virus shows promise for imaging and treating pancreatic cancer**


This AACR press release is also based on a presentation at the Frontiers in Basic Cancer Research meeting. Dana Haddad, MD, PhD, while working at the Memorial Sloan-Kettering, evaluated an oncolytic vaccinia virus encoding the human sodium iodide symporter for its ability to facilitate long-term deep-tissue image monitoring of virotherapy and targeted radiotherapy of pancreatic cancer. Their construct, GLV-1h153, was found to be a promising oncolytic agent for the treatment, long-term imaging, and monitoring of the therapeutic response of pancreatic cancer.

**Inhibition of focal adhesion kinase by PF-562,271 inhibits growth and metastasis of pancreatic cancer**


This *Molecular Cancer Therapeutics* paper out of University of Virginia discusses inhibition of FAK in pancreatic cancer, and phenotypic changes in the tumor cells and microenvironment. PF-562,271 was found to inhibit migration of tumor cells, cancer associated fibroblasts, and macrophages. of mice with PF-562,271 resulted in reduced tumor growth, invasion, and metastases.
Inhibiting Cxcr2 disrupts tumor-stromal interactions and improves survival
Research out of Hal Moses, MD’s lab evaluated a mouse model of pancreatic cancer with an activating mutation of Kras and knockout of TGFβ receptor type II (Tgfbr2). This mouse develops aggressive pancreatic cancer and appears dependent on Cxc family of chemokines. The researchers found that the Cxc chemokines induced connective tissue growth factor expression in the pancreatic stromal fibroblasts, not in the pancreatic ductal adenocarcinoma cells themselves. Treating the mice with a CXCR2 inhibitor blocked pancreatic cancer progression. This study was also written up in Genetic Engineering & Biotechnology News (http://www.genengnews.com/gen-news-highlights/scientists-say-blocking-chemokine-receptor-in-pancreatic-cancer-stromal-cells-helps-slow-cancer-/81245701/).

Nuclear receptor liver receptor homologue 1 (LRH-1) regulates pancreatic cancer cell growth
This PNAS article discusses LRH-1, a regulator of gene transcription, and its newly discovered critical role in pancreatic cancer development and progression.

Zyflamend suppresses growth and sensitizes human pancreatic tumors to gemcitabine
Kunnumakkara et al looked at Zyflamend, a polyherbal preparation with potent anti-inflammatory activities, and its role in sensitizing an orthotopic mouse pancreatic cancer model to treatment with gemcitabine. Their findings suggest that Zyflamend alone has inhibitory activity against pancreatic tumors, and further sensitizes the tumors to gemcitabine.

Toll-like receptor 9 agonist IMO cooperates with cetuximab in K-Ras mutant pancreatic cancer
The authors investigated the combination of Toll-like receptor 9 agonist IMO with the anti-EGFR monoclonal antibody cetuximab in pancreatic and colorectal cancers in vitro and in vivo. Their data suggest that IMO markedly inhibits growth of K-Ras mutant colon and pancreatic cancers in vitro and in nude mice, and cooperates with cetuximab via multiple mechanisms of action.

Hedgehog signaling: Networking to nurture a promalignant tumor microenvironment
This review published in Molecular Cancer Research focuses on the latest findings on the signaling pathways that are activated and/or regulated by molecules generated from Hedgehog signaling in cancer and cites promising clinical interventions, and discusses future directions.

ETIOLOGY
Possible link between two type 2 diabetes drugs and pancreatic cancer, new research suggests
A Gastroenterology paper from July (http://www.ncbi.nlm.nih.gov/pubmed/21334333) picked up considerable media attention in September. Elashoff and colleagues at UCLA evaluated the FDA database of reported adverse events for those associated with glucagon-like peptide-1-based therapy against diabetes. The authors found a significant increase in pancreatitis in patients treated with these types of diabetes drugs, raising concern about subsequent increased risk of pancreatic cancer. Forbes
published an article from the business-end of these studies:

The Lin28/let-7 axis regulates glucose metabolism
Also written up on diabetic live (http://www.diabeticlive.com/diabetes-101/diabetes-news/study-reveals-proteins-linked-to-both-cancer-and-diabetes/), this Cell paper describes a link between proteins involved in cancer and diabetes, with the common pathway being metabolism. The authors’ data establishes the Lin28/let-7 pathway as a central regulator of mammalian glucose metabolism, with roles in cancer formation and onset of diabetes.

Body mass index, abdominal fatness and pancreatic cancer risk
This Annals of Oncology paper describes a systematic review and meta-analysis of prospective studies of the association between BMI, abdominal fatness, and pancreatic cancer risk. The researchers’ findings indicate that general and abdominal fatness increase the risk of pancreatic cancer, and nonsmokers who are considered within the normal BMI range are also at higher risk with increasing BMI.

Pancreatic ductal and acinar cell neoplasms in Carney complex: A possible new association
Gaujoux, et al explored a possible association between pancreatic cancer and Carney complex, a rare disease inherited as an autosomal dominant trait. Carney complex has been associated with various tumors, and is frequently caused by inactivation of the PRKAR1A gene. The authors observed an unexpectedly high prevalence of rare pancreatic tumors among Carney complex patients. Their data suggest that PRKAR1A could function as a tumor suppressor gene in pancreatic tissue, at least in the context of Carney complex patients.

PREVENTION
Fruit and vegetable consumption is inversely associated with having pancreatic cancer
Research out of the laboratory of Gloria Petersen, PhD (Scientific Advisory Board) suggests that consuming certain fruits, vegetables, whole grains, and fiber is inversely related to incidence of pancreatic cancer. These findings may have implications in prevention of this disease.

EARLY DETECTION, DIAGNOSIS, AND PROGNOSIS
MicroRNA-10b expression correlates with response to neoadjuvant therapy and survival
Co-corresponding author on this paper is Lorenzo Sempere, PhD, who cites his 2008 Laurie and Paul MacCaskill – Pancreatic Cancer Action Network – AACR Career Development Award as a funding source for this project. This Clinical Cancer Research paper describes an evaluation of expression of various microRNAs (miR) in pancreatic ductal adenocarcinoma cells. It was found that miR-10b was the most frequently and consistently over-expressed miRNA, compared to its expression in normal pancreatic epithelial cells. Further, miR-10b expression correlated with poor response to cancer therapy, lower
likelihood of surgical resection, and shorter survival. Therefore, miR-10b may be considered a diagnostic and predictive biomarker for pancreatic cancer. Please see commentary on this article featured below.

**microRNA-10b: A new marker or the marker of pancreatic ductal adenocarcinoma?**


George Calin, MD, PhD (2009 Seena Magowitz – Pancreatic Cancer Action Network – AACR Pilot Grant) co-wrote this commentary on the article featured above. The authors describe the importance of this study relating miR10-b to pancreatic cancer, based on the deadliness of the disease, the functional logic of miR10-b’s involvement, the sound methodology, and the high translational potential.

**Test in development can ease cancer concern**


Video:  
http://mediacenter.tveyses.com/downloadgateway.aspx?UserID=46489&MDID=776317&MDSeed=8186 &Type=Media

This story features Max Schmidt, MD, PhD (2003 Pancreatic Cancer Action Network – AACR Career Development Award) and his Indiana University pancreatic cyst clinic (more info: http://pancyst.org/). Dr. Schmidt and colleagues are working on developing a new test whereby a biomarker can determine with 100 percent accuracy if a pancreatic cyst is benign.

**Significance of pathologic response to preoperative therapy in pancreatic cancer**


**Editorial:** Significance of pathologic response to preoperative therapy in pancreatic cancer: The future ain’t what it used to be - http://www.ncbi.nlm.nih.gov/pubmed/21947699

This Annals of Surgical Oncology study (and editorial) discusses whether pathologic response to preoperative therapy may serve as a prognostic marker for pancreatic cancer. Although a strong pathological response to therapy before surgery is rare in pancreatic cancer, those who do respond tend to experience prolonged survival.

**The advancement of biomarker-based diagnostic tools for ovarian, breast, and pancreatic cancer**


Scientists at Pitt review studies involving urine as an analytical biofluid for biomarker development. They highlight findings related to urine-based biomarkers for ovarian, breast, and pancreatic cancer, and compare to biomarker discovery in serum samples.

**Resection status, age and nodal involvement determine survival**


University of Pennsylvania pancreatic cancer patients were retrospectively analyzed for their response to adjuvant 5-FU-based chemoradiation. Findings suggest that resection status, number of involved lymph nodes, and patient age are all significant determinants of patient prognosis.
Immunohistochemical analysis of hENT1 predicts survival in resected pancreatic cancer patients
Published in Annals of Surgical Oncology, this article discusses the relationship between expression of the transporter human equilibrative nucleoside transporter-1 (hENT1) and pancreatic cancer patients’ response to gemcitabine treatment. The authors’ data suggest that high levels of hENT1 represent a good prognostic marker: these patients experienced longer survival after resection and treatment with gemcitabine, consistent with hENT1’s role of transporting the drug into cells.

TREATMENT
Adjuvant chemoradiation therapy after pancreaticoduodenectomy in elderly patients
This study was conducted in the laboratory of Joe Herman, MD (2008 Blum-Kovler – Pancreatic Cancer Action Network – AACR Career Development Award). Dr. Herman and colleagues evaluated the efficacy of adjuvant chemoradiation therapy for pancreatic adenocarcinoma patients ≥ 75 years of age. The authors found that adjuvant therapy after surgery was beneficial towards elderly patients’ 2-year survival, but did not affect 5-year survival. Further examination will determine which patients are best suited for this regimen.

Advances in pancreatic cancer
Diane Simeone, MD (2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant and Scientific Advisory Board member) co-authored this Current Opinion in Gastroenterology review. The article focuses on the relationship between pancreatic cancer cells and tumor stroma, and potential opportunities for therapeutic intervention.

Researcher seeks to defy odds in taking on pancreatic cancer
UC Health featured this article on Dave Dawson, MD, PhD (2008 Seena Magowitz – Pancreatic Cancer Action Network – AACR Career Development Award). Dr. Dawson’s video created by the Pancreatic Cancer Action Network is also included. Dr. Dawson discusses his work on developing personalized care for pancreatic cancer patients, and his focus on understanding and therapeutically targeting pancreatic cancer stem cells.

FOLFIRINOX: A small step or a great leap forward?
Andrew Ko, MD (2003 Pancreatic Cancer Action Network – ASCO Career Development Award) wrote this JCO piece to discuss the implications of the FOLFIRINOX studies that were published recently in the New England Journal of Medicine and presented at the 2010 ASCO annual meeting. The FOLFIRINOX results bring up multiple issues that must be addressed by national cooperative groups and pharmaceutical companies interested in pancreatic cancer drug development. Dr. Ko expresses optimism that these positive clinical trial results bring some change and hope to the field.
Neoadjuvant therapy in pancreatic adenocarcinoma: A meta-analysis of phase II trials
A team of UCLA researchers underwent a meta-analysis examining the best available phase II trials using neoadjuvant treatment for resectable and borderline/unresectable pancreatic adenocarcinoma. Their findings suggest that neoadjuvant therapy is beneficial for borderline/unresectable patients; this treatment has allowed some patients to eventually become surgical candidates. These are the only patients for whom neoadjuvant therapy appears warranted, given current treatment options.

Cationic liposomal paclitaxel plus gemcitabine or gemcitabine alone in advanced pancreatic cancer
Investigators at University Hospital, Mannheim, Germany report on a randomized controlled phase II trial testing paclitaxel embedded in cationic liposomes (EndoTAG™-1; ET). ET is designed to target tumor endothelial cells. Chemotherapy-naïve patients with locally advanced or metastatic pancreatic cancer were randomly assigned to receive gemcitabine or gemcitabine plus ET. The results suggest that treatment of advanced pancreatic cancer with gemcitabine + ET was generally well tolerated and showed beneficial survival and efficacy.

Current immunotherapeutic approaches in pancreatic cancer
Koido et al wrote this *Clinical and Developmental Immunology* review to offer their perspective on how to increase the clinical efficacy of immunotherapies for pancreatic cancer.

The role of autophagy in cancer: therapeutic implications
This review published in *Molecular Cancer Therapeutics* discusses emerging understanding of the role and regulation of autophagy in cancer, and the potential of therapeutically targeting this process.

Immunomedics announces partial clinical hold on clivatuzumab tetraxetan clinical trial
The FDA has placed a partial clinical hold has been placed on Immunomedics’ Phase Ib/II clinical trial of clivatuzumab tetraxetan in patients with advanced pancreatic cancer, due to the administration of an incorrect dose of yttrium-90 to a patient enrolled at one of its trial sites. The trial is fully enrolled, and Immunomedics is working with the FDA to get the partial clinical hold lifted as soon as possible.

CZ BioMed Corp.: Progress in pancreatic cancer cure research – PANRVLYSIN®
CZ BioMed Corp has developed a new compound aimed to treat pancreatic cancer. PANRVLYSIN® is a novel, genetically-engineered oncolytic virus that selectively targets cancer cells. CZ BioMed is interested in partnering with bio-pharma companies and is initiating the process of applying for IND (investigational new drug) status from the FDA, to embark on Phase I clinical trials.
Arch Biopartners identify lead compound for pancreatic cancer and non small cell lung cancer
Arch Biopartners Inc has identified GH501a as a lead compound for development in the treatment of non-small cell lung cancer and pancreatic cancer, based on promising preclinical results. The announcement does not discuss the drug’s mechanism of action.

Rexahn Pharmaceuticals advances pancreatic cancer drug
Rexahn Pharmaceuticals announced enrollment of metastatic pancreatic cancer patients for its Phase II trial of Archexin, an Akt inhibitor. Rexahn expects to report results of the trials in the first half of 2012.

MedImmune inks deal for Pfizer's anticancer mAb therapeutic
Tremelimumab, a fully human mAb that binds to the protein CTLA-4, was tested by Pfizer in Phase I studies to determine toxicity in chemo-naïve patients with metastatic pancreatic cancer. MedImmune will now assume global development rights to tremelimumab.

Novartis drug Afinitor® gains EU approval to treat advanced pancreatic neuroendocrine tumors
Afinitor® was approved by the US FDA to treat advanced pancreatic neuroendocrine tumors in May 2011. Now, the drug has been approved for this indication in all 27 European Union member states, plus Iceland and Norway. Afinitor® targets mTor, a protein known to be active in many cancer types and regulates tumor cell division, metabolism, and blood vessel growth.

Unpublished phase III cancer trials: Eliminating the negative?
http://www.cancer.gov/ncicancerbulletin/092011/page6
The NCI Cancer Bulletin published this article, describing “Compendium of unpublished phase III trials in oncology: characteristics and impact on clinical practice” (http://www.ncbi.nlm.nih.gov/pubmed/21747079). Tam et al reported that nearly one in ten phase III trials presented in abstract form at the ASCO annual meeting remained unpublished more than six years later. Most of these unpublished studies had negative or inconclusive results. As negative results can still be informative to the design of future trials and moving the field forward, the authors offer solutions such as a journal devoted to negative clinical trial reports, or encouragement of mainstream journals to publish short reports on clinical trials with negative outcomes.
CANCER CONTROL, SURVIVORSHIP, AND OUTCOMES RESEARCH
Perineural invasion and associated pain in pancreatic cancer
Published in *Nature Reviews Cancer*, T-Gen researchers discuss the potential of targeting the pathways and signaling molecules involved in perineural invasion, pain, and aggressive tumor behavior.

Pain in pancreatic cancer: Does drug treatment still play a role?
http://www.joapl.net/prev/201109/15.html
This editorial in the *Journal of the Pancreas* discusses pain management in pancreatic cancer patients.

Cancer patients at risk for serious blood clots: study
Work presented at the European Multidisciplinary Cancer Congress in Stockholm suggested that blood clots affect as many as one in five US cancer patients. One year after treatment, the risk of getting a venous thromboembolism was highest among pancreatic cancer patients, at 21.5 percent.

Incidence of pancreatic adenocarcinoma in patients with a history of nonpancreatic primary cancers
Researchers at Columbia University and New York Presbyterian Hospital analyzed SEER data and discovered that there is an increased risk of subsequent pancreatic cancer after diagnosis with another type of cancer, with results varying among patients of different age groups.

Information of imminent death or not: Does it make a difference?
This *Journal of Clinical Oncology* study looked at the difference between cancer patients who were informed that they were at their end of life, and patients who were not informed. There was no change in symptom control, pain, or anxiety, but informing patients of the terminal nature of their diagnoses was associated with improved care and increased the likelihood of fulfilling the principles of a good death.